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Table of Contents.

ORIGINAL ARTICLES— Page.

Some Observations on the Cardiac Output and its Measurement, with a Description of a Modified Carbon Dioxide Method, by M. J. Morrissey and A. Jean Palmer .. 113

Surgical Treatment of Urinary Infections, by Arthur Carrodus .. 118

Observations on the Effect of High Fat Diet in Alloxan Diabetic Rats, by J. Bornstein and J. F. Nelson .. 121

Deafness following Maternal Rubella, by N. E. Murray .. 126

The Over-Emphasis on Psychiatric Symptoms, by S. J. Minogue .. 130

Some Problems Concerning the Ætiology of Rheumatic Fever, by Sydney D. Rubbo .. 133

A Hæmagglutination Test for the Diagnosis of Influenzal Meningitis, by M. F. Warburton and E. V. Keogh and S. W. Williams .. 135

Congenital Steatorrhœa due to Defect of the Pancreas, by Margaret Harper .. 137

REVIEWS—

Correlative Neuroanatomy .. 141

Chest Examination .. 141

Blood Derivatives and Substitutes .. 142

Epilepsy .. 142

BOOKS RECEIVED .. 142

LEADING ARTICLES—

History and Australian Medicine .. 143

CURRENT COMMENT— Page.

The Intravenous Administration of Iron .. 144

The Prognosis of Exudative Pleurisy in Children .. 144

A New Treatment of Alcoholism .. 145

ABSTRACTS FROM MEDICAL LITERATURE—

Physiology .. 146

Biochemistry .. 147

Medicine .. 147

BRITISH MEDICAL ASSOCIATION NEWS—

Scientific .. 148

MEDICAL SOCIETIES .. 149

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—

Queensland .. 150

OBITUARY—

James Sprent .. 150

Reginald Arthur Parker .. 151

James Macdonald Gill .. 152

Keith McKeddie Doig .. 152

Clive Henry Sippe .. 152

NOMINATIONS AND ELECTIONS .. 152

NOTICE .. 152

MEDICAL APPOINTMENTS .. 152

DIARY FOR THE MONTH .. 152

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 152

EDITORIAL NOTICES .. 152

SOME OBSERVATIONS ON THE CARDIAC OUTPUT AND ITS MEASUREMENT, WITH A DESCRIPTION OF A MODIFIED CARBON DIOXIDE METHOD.

By M. J. MORRISSEY AND A. JEAN PALMER.

From the Department of Medicine, the University of Sydney.

WILLIAM HARVEY discovered the circulation of the blood in 1628, and though more than three centuries have elapsed since then, it has been only in the last three decades that any sustained work has been done on its quantitative measurement. Yet, despite this later concentrated effort, the cardiac output still remains a quantity not easy to measure exactly.

The application of Fick's principle requires as data the gaseous exchange per minute in millilitres of either oxygen or carbon dioxide and the corresponding arterio-venous difference in volumes *per centum*. The cardiac output can then be calculated from the following equation:

$$\text{Cardiac output per minute} = \frac{\text{Gaseous exchange per minute in millilitres}}{\text{Arterio-venous difference in volumes } \textit{per centum}}$$

There are certain difficulties in regard to obtaining the data for gaseous exchange. This will be referred to in some detail later on in this paper. It is in the determination of the arterio-venous difference for either oxygen or carbon dioxide that the principal technical difficulty is encountered. Arterial puncture, under local anæsthesia, has now become a routine procedure in many laboratories, and the blood so obtained, with due precaution to avoid contact with air, should yield on analysis valid figures for the gaseous content of the arterial blood. However, in order to determine the arterio-venous difference, the gaseous content of the venous blood must also be known accurately. The term "venous blood" here connotes the mixed venous blood of the right side of the heart, for, as is well known, the gaseous content of blood from individual veins varies greatly according to the metabolic state of the region from which they drain. Samples of this blood have been obtained by direct heart puncture,[10][12] but there is an obvious risk involved in this. Samples of the mixed venous blood can also be obtained by the technique of catheterization of the right side of the heart first performed on himself as subject by Forssmann,[11] and developed by Cournand and Ranges,[4] by their co-workers,[5][6][7][8][9] by Stead, Warren Merrill and Brannon[24][3][25] and by McMichael and his colleagues.[1][15][16][17][23][28] In the aggregate thousands of such catheterizations have now been performed. Though no untoward incident has been reported, there are some nominal drawbacks consequent upon the thrombus which sometimes forms about the point of entry of the catheter into the medial ante-cubital vein. In this laboratory this method has not been tried on human subjects, but one of us (A.J.P.) has successfully applied it to sheep, the portal of entry being the external jugular vein. In working out results from the "right heart" catheterization technique, figures for oxygen consumption and arterio-venous difference are usually taken in preference to the corresponding carbon dioxide figures, because of the reputed lability of these latter figures. This greater variability, if any, would be probably due to the greater physiological diffusibility of carbon dioxide.

This laboratory has been engaged for some time past on the investigation of the carbon dioxide method[29] for cardiac output in which the necessary data are obtained indirectly from respiratory procedures. Set out as above, the required data are: (i) the carbon dioxide production per minute; (ii) the carbon dioxide level in the arterial blood; (iii) the carbon dioxide level in the venous blood. The first of these is arrived at from collection and analysis of the expired air, the second from analysis of the alveolar air, and the third from a rebreathing procedure in which

a mixture of carbon dioxide in oxygen is used, the concentration of carbon dioxide varying from 9% to 10%. It is evident that in principle the method is a modification of the original carbon dioxide method of Douglas and Haldane.[10]

Details of Method.

The apparatus which was originally devised to obtain these data required the cooperation of the subject and the proximity of the operator to the subject. It was obvious that it would be a distinct advantage if alveolar samples could be obtained without the cooperation of the subject, or better still without his prior knowledge, as thinking about one's respiration inevitably alters its rate, depth and character. It was also desirable that the operator be able to control the procedure at a distance from the subject. An apparatus fulfilling these requirements was devised and has been described in detail elsewhere.[13] A ground plan is shown in Figure I of this paper. In brief, the apparatus consists of a series of valves worked by a series of electromagnets, which open and shut the valves according to the position of a switch. By this means the subject's respirations can be instantly diverted from one valve through another. This switching can be carried out from a distance, even from another room if it is considered necessary. This remote control was instituted so as to reduce to a minimum any interference with the patient's basal state.

To collect the expired air valve R_1 is maintained in the open position, the patient's expirations thus being directed through the air-outlet attached to this valve to a Douglas bag.

The alveolar air is obtained by a method based on that of Haldane and Priestley,[12] but instead of the patient's having to make an active maximal expiration, air is drawn off from the lungs by suction created by the dropping of a weighted piston within a cylinder. This is achieved by turning the control switch through one stage, thereby closing valve R_1 and opening valve R_2 and causing the piston (not shown in Figure I) to drop. The suction is quite sufficient to draw off the subject's tidal and supplemental air into the cylinder, although the actual negative pressure is so slight that, if it were not for the interposing of the one-way valve ("I" in Figure I), the subject could easily lift the piston and weight by an inspiratory effort. The drawing off of the tidal and supplemental air causes the respiratory and instrumental dead spaces to be filled with air from the alveoli. Two samples of this alveolar air are taken by turning the switch through the next two stages, thus closing valve R_2 and opening and closing valves V_1 and V_2 in succession. The opening of valves V_1 and V_2 allows the filling of the evacuated gas sampler attached to each of them. It should be noted that since the valves open and close in succession, the gas sampler attached to V_1 is filled and closed off before that attached to V_2 is opened. The samples thus obtained are not taken simultaneously but consecutively. It is considered that true alveolar air has been obtained when subsequent analysis shows close agreement between the two samples. If there is any contamination with dead space air, there will be an upward gradient of carbon dioxide and a downward gradient of oxygen between the first and second samples.

The final step is the rebreathing procedure. No inspiration is possible after the alveolar sampling until the switch is turned to open valve R_3. The opening of this valve connects the patient with a rebreathing bag, which contains two to three litres of a mixture of approximately 9% to 10% of carbon dioxide in oxygen. The patient rebreathes this mixture for seven or eight breaths, samples being taken at the fifth and eighth breaths through valves V_3 and V_4 respectively. If on analysis these two samples agree in their carbon dioxide content, that fact denotes that equilibrium has been reached in the lung-rebreathing bag system. In other words, a plateau has been reached in the duration of which there is neither a giving-off of carbon dioxide to the lung spaces nor an absorption of the gas by the blood from these spaces. It should be noted that the carbon dioxide tension thus obtained is the "virtual venous" tension, because the oxygen tension in the lung-rebreathing bag system remains so high (300 millimetres approximately) that the blood remains oxygenated, though it retains its venous carbon dioxide content.

A valid objection has been raised to many indirect methods for determining the cardiac output previously in use, in that the procedure could not be completed within one circulation time. Recirculation of the rebreathed gases occurred, leading to an erroneously high figure for the arterio-venous difference and a correspondingly low figure for the cardiac output. In the method described above, each step follows the previous step smoothly and automatically, the maximum time elapsing from the opening of valve R_2 to the closing of valve V_4 being twelve seconds.

When the tensions for the alveolar and "virtual venous" carbon dioxide have been obtained, they are applied to the dissociation curve for the patient's own blood, and the corresponding carbon dioxide content in volumes *per centum* is determined. It has been found convenient to

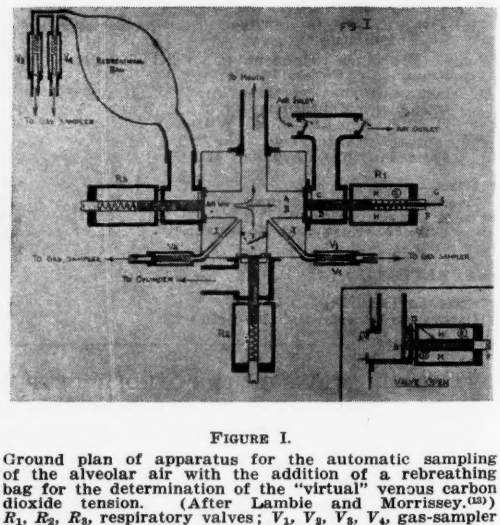

FIGURE I.

Ground plan of apparatus for the automatic sampling of the alveolar air with the addition of a rebreathing bag for the determination of the "virtual" venous carbon dioxide tension. (After Lambie and Morrissey.[13]) R_1, R_2, R_3, respiratory valves; V_1, V_2, V_3, V_4, gas-sampler valves; *A*, rubber valve seating; *B*, base of iron plunger type valve; *C*, rubber buffer; *D*, body of plunger valve; *E*, metal spring; *F*, metal stop for spring; *G*, extension for manually operating valve; *H*, coil solenoid; *I*, accessory valve; *J*, channel from gas samplers to airway; *M*, main body of valve.

use the equations derived by Parsons[21] and to calculate the blood carbon dioxide content directly. Since, at least in normal subjects, the alveolar air is considered to be in equilibrium with the arterial blood, the difference between these two figures gives the arterio-venous difference and this divided into the gaseous exchange gives the cardiac output.

Procedure with Subject.

The subjects used were either members of the staff of the medical school of the University of Sydney or medical students, and they presented themselves in the morning in the fasting state. They were placed on a bed in a semi-recumbent position and allowed to rest for at least half an hour. During this period the valves were tested for possible leaks and evacuated gas samplers were attached to the smaller valves V_1, V_2, V_3 and V_4 by heavy pressure tubing. Latterly, since it was so small, no special pains were taken to evacuate the dead space between the valve seating and the gas samplers. The rebreathing bag was filled with the desired gas mixture, and a Douglas bag for the collection of the expired air was attached to the air inlet through a two-way valve. The valve plunger in R_1 (Figure I) was held open by a metal clip.

No instructions were given to the subject about the alveolar air, except to advise him that a slight suction would be felt during the course of the experiment. With regard to the rebreathing, the only instruction given was to breathe fast and deeply when told to do so.

The expired air was collected over a period of five minutes. The electric circuit (40 volts direct current) was then turned on and alveolar and rebreathing samples were taken, attention being paid to the following points: (i) All alveolar samples were taken at the end of a normal expiration. (ii) The first experiment of the day for any one subject was used as a pilot experiment, to ascertain the optimal volume of gas mixture to be placed in the rebreathing bag and the optimal concentration of carbon dioxide in that mixture. Both these factors vary from one subject to another, the volume depending mainly on the size of the subject, and the concentration of carbon dioxide depending on the level of that gas in the subject's venous blood. (iii) The experiment was repeated until satisfactory samples of both alveolar air and "virtual venous" air were obtained in the same experiment. This generally meant two or three experiments, including the pilot experiment. In order to suit laboratory convenience, it was customary during the earlier part of this work to allow the subject to leave at this point, blood for the production of the dissociation curve being obtained by venepuncture on some later day. This procedure was found to introduce a fallacy, owing to the labile position of the carbon dioxide dissociation curve under the influence of food and exercise. In all the experiments reported in this paper, venepuncture was performed on the subject whilst still in the basal state and lying on the bed.

The blood was equilibrated[(20)] with two different carbon dioxide and oxygen mixtures. The proportions of carbon dioxide in these mixtures were accurately determined in the Haldane apparatus. They usually amounted to approximately 5% and 10% respectively. The remainder of the gas present being oxygen, the blood when equilibrated was fully oxygenated. Samples of the equilibrated blood were analysed for their carbon dioxide content in the Van Slyke-Neil apparatus. The position of two points on the carbon dioxide dissociation curve was thus determined by analysis, and the remainder could then be calculated by the method of Parsons. This curve referred to fully oxygenated blood.

Analysis of the alveolar air samples gave the tension of carbon dioxide in the arterial blood. Similarly, from the rebreathing samples the "virtual venous" carbon dioxide tension was found. Reference to the dissociation curve gave the corresponding carbon dioxide contents in volumes *per centum*, the difference between these two figures being the arterio-venous difference. The gaseous exchange divided by the arterio-venous difference gave the cardiac output in litres per minute.

The results obtained are shown in Table I. As was mentioned above, they do not include those subjects from whom the blood samples were taken on a day different from that on which the respiratory samples were taken.

In this group the general tendency of the change in position of the dissociation curve was to produce an apparent lowering of the cardiac output. It will be seen that the figures for the cardiac index fall between 2·0 and 3·7 litres per square per minute. This falls well within the limits found by other workers cited above; but it may well be asked whether such a wide variation among normal individuals is in fact a real one, or whether it is not partly adventitious.

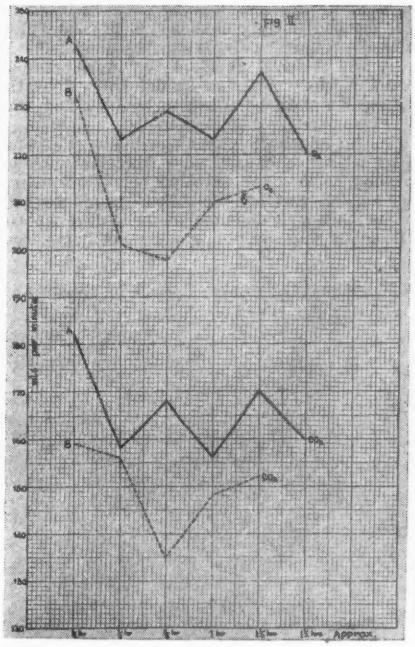

FIGURE II.

Graph showing variation in carbon dioxide production and oxygen consumption of two subjects, A and B, in the resting state, determined on the same morning, with approximately a quarter of an hour's difference between the determinations.

Discussion.

In all methods there is a margin of error in the determination of the basal cardiac output, which is difficult

TABLE I.

Name of Subject.	Sex.	Pulse Rate per Minute.	Respirations per Minute.	Gaseous Exchange, Carbon Dioxide. (Millilitres per Minute.)	Gaseous Exchange, Oxygen. (Millilitres per Minute.)	Respiratory Quotient.	Surface Area. (Square Metres.)	Basal Metabolic Rate. (Percentage Variation.)	Alveolar Carbon Dioxide. (Millimetres of Mercury.)	"Virtual Venous" Carbon Dioxide. (Millimetres of Mercury.).	Volumes *per Centum* of Carbon Dioxide Venous.	Volumes *per Centum* of Carbon Dioxide, Arterial.	Arterio-Venous Carbon Dioxide Difference. (Vols. *per Centum*.)	Cardiac Output. (Litres per Minute.)	Cardiac Index. (Litres per Square Metre per Minute.)	Stroke Output. (Millilitres.)
A.H.	M.	60	12	200	228	0·88	1·8	−2	39·4	49·5	55·1	50·3	4·8	4·2	2·4	70
J.I.	M.	70	10	187	246	0·76	1·8	−5	43·7	50·9	55·2	52·3	2·9	6·4	3·5	91
A.P.	F.	60	16	160	209	0·77	1·7	−5	39·6	48·2	53·6	49·5	4·1	3·9	2·3	68
W.B.	M.	72	16	182	252	0·72	2·0	−16	39·7	49·6	51·9	47·3	4·6	4·0	2·0	56
G.D.	M.	60	8	218	261	0·83	2·2	−15	42·0	48·2	59·3	56·2	3·1	7·0	3·2	116
G.P.	M.	54	10	185	248	0·74	1·7	±0	41·1	48·7	58·4	54·9	3·5	5·3	3·1	98
T.W.	M.	62	14	201	272	0·74	1·9	+2	43·8	51·8	58·0	54·1	3·9	5·2	2·8	84
P.H.	M.	58	14	187	246	0·76	1·9	−10	42·6	48·5	53·1	50·3	2·8	6·7	3·5	115
B.A.	F.	67	13	158	205	0·77	1·6	+2	39·8	48·8	45·5	41·7	3·8	4·2	2·6	63
B.Mc.	F.	75	13	144	180	0·8	1·6	−9	37·5	46·7	50·9	47·3	3·6	4·0	2·6	53
T.H.	M.	60	13	183	235	0·78	1·9	−12	44·4	50·8	54·0	51·3	2·7	6·8	3·7	113
J.W.	F.	70	13	136	203	0·67	1·5	±0	38·1	47·5	49·6	45·6	4·0	3·4	2·2	57

to evaluate quantitatively, being due on the one hand to intrinsic experimental error and on the other to a complex of psychological and physiological factors in the subject. The latter factors vary from patient to patient and make it well-nigh impossible to compute an over-all probable error.

In Table I we have not given the cardiac output to a greater degree of accuracy than to the nearest hundred millilitres per minute; but in some cases at least, in which the subject seemed unduly nervous, it is doubtful whether such inferred accuracy as this can be justified. In some subjects even in the resting state the oxygen consumption and carbon dioxide production as determined by the usual methods appear not to be constant, but to fluctuate, as is shown in Figure II.

The subjects of these experiments were members of the medical school staff and were familiar with the technique involved, so that the question of variation in gaseous exchange due to anxiety or other psychological cause should be of minor importance. The time of collection of each Douglas bag sample was five minutes, and there

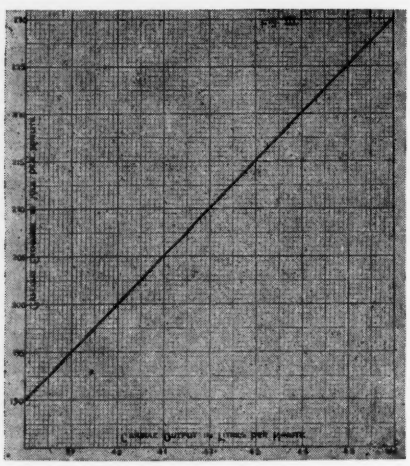

FIGURE III.

Variations which can occur in the computed cardiac output as a result of change in gaseous exchange per minute, the arterio-venous difference being considered constant at five volumes *per centum* (hypothetical).

was approximately fifteen minutes' interval between the experiments. From Figure II it can also be seen that the apparent oxygen consumption is just about as labile as the carbon dioxide production in these two subjects.

In the modified carbon dioxide method for cardiac output as outlined above, the respired gases are collected immediately before the other respiratory samples, and in the computing of the cardiac output the arterio-venous difference is related to a gaseous exchange slightly anterior to it in time.

Admittedly this is not an ideal procedure; but the subject does lie quiet and undisturbed throughout. On the other hand, with the "right heart" catheterization method it is possible to collect the expired air over a period of time roughly simultaneous with the collection of the blood samples. This approaches more closely to the ideal of simultaneity in obtaining values for both factors of the Fick equation; but in some subjects at least such an amount of experimental procedure going on would interfere with the basal state. In such circumstances the figures obtained would indeed be a true index of the cardiac output at the time of the experiment, but would be somewhat elevated according to the reaction of the subject to the experimental procedures.

However, if in the endeavour to approach simultaneity in collecting both blood and expired air the time of the collection of the expired air is cut too short, then the difficulty of measuring its volume accurately is much increased. There is an optimum time for the collection of the expired air, for if, on the other hand, the period of collection is too long, the noseclip becomes irksome to the subject, who grows increasingly restless.

As a rather extreme example of what may happen when the time of collection is rather short, suppose that the subject is breathing slowly at the rate of 8·5 respirations per minute, and that the volume of each respiration is approximately 500 millilitres. If the time of collection is precisely one minute, then a portion, if not the whole, of one expiration may be missed. This may represent an oxygen consumption of some 30 millilitres, and according to the respiratory quotient, a corresponding carbon dioxide production. A variation much less in extent than this can cause an appreciable difference in the computed cardiac output, as will presently be shown. If care is taken to commence and to end the collection of the expired air at the same phase of respiration, this source of error can be eliminated. If the precise time of collection is noted, a simple calculation will give the respiratory

TABLE II.[1]

Gaseous Exchange. (Millilitres per Minute.)	Cardiac Output. (Litres per Minute.)
190	3·8
195	3·9
200	4·0
205	4·1
210	4·2
215	4·3
220	4·4
225	4·5
230	4·6

[1] See Figure III.

TABLE III.[1]

Arterio-Venous Difference. (Volumes *per Centum.*)	Cardiac Output. (Litres per Minute.)
5·0	4·0
5·1	3·92
5·2	3·85
5·3	3·77
5·4	3·70
5·5	3·64
5·6	3·57
5·7	3·51
5·8	3·45
5·9	3·39
6·0	3·33

[1] See Figure IV.

minute volume. Even so, we are still beset with variation, for as is well known, the rate, the volume of each respiration and the respiratory minute volume may all come within this category in the one subject under the strictest basal conditions. On the other hand, if the period for the collection of the expired air is too prolonged, as was mentioned above, the mouthpiece and noseclip become increasingly irksome to the patient with consequent restlessness and increase in metabolic rate.

The gaseous exchange will apparently vary in the same subject on one and the same morning, as is shown in Figure II. While it is true that a variation in the gaseous exchange will have no effect on the computed cardiac output provided that the arterio-venous difference varies *pari passu* with it, there is no evidence to suggest that this is so.

Variations in Computed Cardiac Output.

The precise extent of the physiological variation in cardiac output is somewhat obscured by the fact that a relatively small variation in gaseous exchange can cause quite surprising differences in the computed cardiac

output. In this regard McMichael and Sharpey-Schafer[18] consider that a change in cardiac output of 0·4 litre per minute or more may be regarded as significant.

In Figure III and Table II, from which it is derived, are set out the variations which can occur in cardiac output when the gaseous exchange alters. In this hypothetical case the arterio-venous difference is considered constant at five volumes *per centum*. It can be seen that a variation of only 10 millilitres per minute in the gaseous exchange will cause a variation of 0·2 litre in the computed cardiac output. From Figure II it can be seen that an apparent physiological variation of such a magnitude, which after all is relatively small, is not to be unexpected even in trained subjects in the resting state. Added to this physiological variation there may be another arising from the difficulty of accurately measuring the respiratory volume over short periods of time. A total variation from the true figure for gaseous exchange of only 20 millilitres per minute would result in a variation of 0·4 litre per minute in the cardiac output.

One sometimes sees in published work a statement to the effect that "the cardiac output was 5·15 litres per minute". To those working in this special field this is an

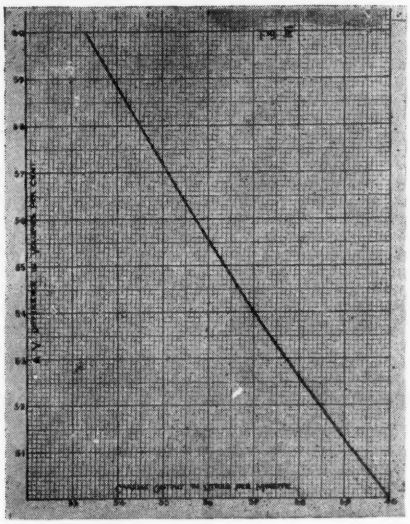

FIGURE IV.

Variations which can occur in computed cardiac output as a result of change in arterio-venous difference, the gaseous exchange per minute remaining constant at 200 millilitres per minute (hypothetical).

obvious arithmetical gloss, but others may be tempted to interpret it literally. If a strict interpretation is placed upon such a statement made without qualification, then it would be taken to mean that the cardiac output was indeed 5·15 and not 5·14 or 5·16 litres per minute. In the hypothetical case given above, in order to compute the cardiac output to the second decimal place (that is, to within 10 millilitres per minute) it would also be necessary to determine the gaseous exchange to 0·5 millilitre per minute—that is, if it is assumed that the arterio-venous difference remained constant at five volumes *per centum*.

It is also of interest to compute in a similar hypothetical instance the difference in cardiac output which would follow a variation in the arterio-venous difference, by hypothesis the gaseous exchange remaining constant at 200 millilitres per minute. A somewhat similar graph is set out by Stead, Warren, Merrill and Brannon;[34] but Figure III is more concerned with small differences such as might fall within the category of experimental error.

Though the graph published herewith (Figure IV, and Table III) is not a straight line, it is very nearly so over this range, and it can be seen that a variation in the arterio-venous difference from 5·0 to 5·1 volumes *per centum* (that is, one millilitre per litre) results in a variation of 80 millilitres in the computed cardiac output. To be able to compute the cardiac output to 10 millilitres it would be necessary, assuming a constant gaseous exchange of 200 millilitres per minute, to determine the arterio-venous difference to within 0·0125 volume *per centum*.

Conclusion.

Such are a few of the difficulties, technical and theoretical, involved in the practical application of the Fick principle to the determination of the cardiac output. Workers in the special field are cognizant of these limitations. Warren, Brannon and Stead[36] have published a critical analysis of the "right heart" catheterization method. This present paper has dealt with the problem in a more general way, though by no means exhaustively.

Summary.

1. A modified carbon dioxide method for determining the cardiac output is described.

2. The results are given for the cardiac output in twelve normal subjects under basal conditions. The cardiac output per square metre of body surface per minute—that is, the cardiac index—varied from 2·0 to 3·7 in these subjects.

3. Some of the sources of error and technical difficulties inherent in all methods based on the Fick principle are discussed. It is shown that the computed cardiac output is the resultant of physiological, psychological and experimental factors.

Acknowledgements.

For many helpful criticisms and suggestions we wish to thank Professor C. G. Lambie, under whose direction this work was carried out. We are indebted to Mr. R. B. Dunphy for the illustrations and to Mr. S. Woodward-Smith for their reproduction. To those who gave so generously of their time to act as subjects we owe a special debt. We also wish to thank Dr. J. T. Tyrer for his help in some of the experiments.

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SURGICAL TREATMENT OF URINARY INFECTIONS.[1]

By ARTHUR CARRODUS,
Sydney.

URINARY TUBERCULOSIS.

THE diagnosis of urinary tuberculosis rests on the finding of tubercle bacilli in the urine. Medlar[1] has demonstrated conclusively that tubercle bacilluria always means infection of the genito-urinary tract. Further investigation shows whether the disease is unilateral or bilateral. In unilateral renal infections treatment is radical—namely, nephrectomy. Conservative measures such as sanatorium treatment alone give uniformly poor results. At nephrectomy particular care is taken to prevent soiling of the wound with infected contents of the pelvis or ureter, especially in cases of tuberculous pyonephrosis. As much of the ureter as possible is removed and the stump is treated with carbolic and alcohol. If the wound happens to be soiled with tuberculous urine, then breaking down of the wound with prolonged convalescence may occur. Such cases are rarely encountered these days. Recent reports indicate that these sinuses heal readily with streptomycin treatment.

With bilateral infections, the disease is usually much more advanced in one kidney. When one kidney is non-functioning and pyonephrotic and associated with pain, the removal of that kidney often results in a great improvement in the general condition. This is often seen in patients with associated pulmonary or bone and joint infection. Rarely does the infected ureteral stump cause any trouble. Occasionally a pyoureter or empyema of the ureter results, necessitating ureterectomy.

After nephrectomy for unilateral renal tuberculosis, the vesical infection usually heals spontaneously, though this may take months or even years, depending on the intensity of the infection. Hanley,[2] in a review of the post-operative results in 200 cases of nephrectomy, found that in the tuberculosis cases the vesical symptoms might persist as long as eight years after operation, and 30% of those patients still passed tubercle bacilli in the urine five years after nephrectomy. Redewill[3] reported two cases of vesical tuberculosis cured by streptomycin (one gramme per day for six weeks).

A little later the following two patients were treated with streptomycin at the Repatriation General Hospital, Concord, in association with Dr. A. W. Morrow and Dr. Karen Helms.

CASE I.—Left nephrectomy for tuberculosis was performed in December, 1946. The patient was readmitted to hospital in July, 1947, with a seven-months history of scalding and frequency of micturition, urine being passed every quarter to half an hour during the day and hourly at night. Microscopic examination of the urine by direct smear revealed many polymorphonuclear cells and acid-fast bacilli. The right kidney appeared normal in an excretion urogram. The X-ray films of the chest revealed a minimal lesion at the apex of the right lung. Cystoscopy revealed the typical picture of vesical tuberculosis with ulceration at the fundus and a capacity of only four ounces. Clinically this patient had residual vesical tuberculosis with a contracted bladder. Streptomycin was given, two grammes per day in divided doses, every three hours for six weeks—a total of 83 grammes. The acid-fast organisms rapidly disappeared from the urine and the pyuria was relieved. On the completion of treatment there was no scalding on micturition and the frequency had been reduced to the passage of urine hourly day and night. With such a contracted bladder, this was regarded as satisfactory. Six months later, the urine was found to contain only an occasional cell. A year after treatment there was still no scalding, urine was still passed hourly, and the patient's general condition was good. The beneficial effects of streptomycin treatment had been maintained for one year, and the vesical tuberculosis was regarded as cured.

CASE II.—The second patient had pulmonary tuberculosis, left pyonephrosis and an apparently normal right kidney. Left nephrectomy was performed in February, 1947. The right kidney urine was later found by guinea-pig test to contain tubercle bacilli. About seven months later the vesical symptoms were still troublesome. At this time the right kidney still appeared normal in an excretion urogram. At cystoscopy, an area of ulceration was seen on the left lateral wall of the bladder. Pronounced pyuria was present. In October, 1947, streptomycin treatment was commenced; streptomycin was given in divided doses, two grammes per day for sixty days, a total of 120 grammes. Rapid relief of vesical symptoms occurred. In January, 1948, two months after completion of the treatment, cystoscopy revealed a normal bladder except for an area of scarring at the site of the previous ulceration. There was no scalding on micturition, and urine was passed six times during the day and not at all during the night. Five months after treatment the urine contained only an occasional leucocyte. The patient was last examined in July, 1948, nine months after commencement of treatment, and was still symptom-free; there was no scalding on micturition, and urine was passed six to eight times a day and not at all at night. Examination of the urine revealed sterile pyuria.

In this case the symptomatic improvement has been maintained for nine months. The vesical tuberculosis is regarded as cured. The patient probably still has a minimal lesion in his remaining kidney.

In December, 1947, Slotkin[4] reported six cases of inoperable bilateral renal tuberculosis treated with a combination of "Moogrol" (40 millilitres—ethyl ester of hydnocarpus oil) and streptomycin (30 grammes) over thirty days, with remarkable improvement clinically, bacteriologically and cystoscopically. In-vitro experiments indicated that chaulmoogra oil and its derivatives dissolved the waxy envelope of the tubercle bacillus, rendering it more susceptible to streptomycin. In March, 1948, at the Repatriation General Hospital, Concord, a patient suffering from vesical tuberculosis and a tuberculous cavity

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on August 26, 1948.

in his remaining kidney was treated in this manner, with marked symptomatic improvement.

Streptomycin has a definite place in the treatment of urinary tuberculosis. This is so even when the disease is bilateral and inoperable, as it can alleviate bladder symptoms and make life more tolerable. The most dramatic change is in the cystoscopic appearance—from the typical picture of vesical tuberculosis to a normal bladder in six to eight weeks. Acid-fast bacilli rapidly disappear from the urine, sometimes within a week, probably owing to the sterilizing action of streptomycin, as the vesical ulcers take a month or more to heal. With regard to symptoms, scalding on micturition disappears quickly. Frequency of micturition depends on the vesical capacity. When this is not much reduced, then the frequency is relieved as the ulcers heal. Not much reduction in the frequency can be anticipated with the markedly contracted bladder following interstitial cystitis.

From the evidence now available, one may say with confidence that streptomycin will cure residual vesical tuberculosis, the bladder healing in six to eight weeks. When interstitial cystitis has been present, a contracted bladder with frequency of micturition persists. A condition similar to Hunner's cystitis sometimes occurs, and benefit is obtained from diathermy and hydrostatic dilatation. There is no evidence to date that streptomycin can cure renal tuberculosis. In fact, all the evidence—clinical, bacteriological and pathological—indicates that streptomycin does not cure renal tuberculosis. When it is used in the treatment of bilateral renal tuberculosis or of tuberculosis in a solitary kidney, in the majority of cases the patient's condition shows a dramatic improvement because of the healing of the vesical tuberculosis and relief of bladder symptoms. The pyuria becomes less and may disappear. The tubercle bacilluria disappears early, owing to the sterilizing action of the streptomycin. However, after a varying period, usually months, perhaps a year, the pyuria returns, and then tubercle bacilli are again found in the urine and symptoms may recur owing to reinfection of the bladder. Cook and Greene[5] reported fifteen cases of urinary tuberculosis of various types; the patients had been treated with streptomycin and observed for varying periods. One patient had been observed for two and a half years, and he had received in all 500 grammes of streptomycin. They were satisfied that in only three patients was the disease definitely arrested. These workers also had the opportunity of studying five kidneys removed after streptomycin therapy. In four there was no evidence of a reparative process which could be ascribed to streptomycin alone. In the fifth kidney there was an unusual fibrotic process which they did not consider to be due to streptomycin. Streptomycin is not a substitute for surgery, but a helpful adjunct. It has been described as a "step forward in the treatment of urinary tuberculosis, but only a step in a long stairway". As the drug becomes cheaper, it will probably be used after nephrectomy for the routine treatment of the residual vesical tuberculosis.

Non-Tuberculous Infections of the Urinary Tract.

In the discussion of non-tuberculous infections of the urinary tract, it should be understood that the medical forms of treatment—for example, the sulphonamide drugs, antibiotics, urinary antiseptics and acidifying agents, and dietary measures—are used either prior to or in association with surgical treatment. The greatest advance in treatment in recent years has been the use of streptomycin, and already several hundred cases have been reported of the successful use of this drug in the treatment of pyelitis and pyelonephritis due to *Bacillus coli communis*, *Bacillus proteus* and *Bacillus pyocyaneus*.

From the surgical aspect certain points need comment.

1. Alkalinization of the urine is recommended. Excess alkalinity should be avoided in urea-splitting infections (for example, *Bacillus proteus*), as it favours bacterial growth and precipitation of phosphates. This is important in encrusted cystitis and recurrent calculous disease. In these infections, the urine is alkaline enough.

2. From the surgical aspect the most important point is that obstruction must be dealt with and foreign bodies removed before or during therapy before a successful result can be obtained. In the cases reported, it appears that indwelling urethral catheters, ureteral splints, suprapubic tubes and nephrectomy tubes predispose to the persistence of infection and the development of streptomycin resistance. Streptomycin may produce a temporary sterilizing action in the presence of these foreign bodies, but infection soon recurs, so the sooner they can be dispensed with the better.

Persistent and Recurrent Urinary Infections.

What are the factors responsible for persistent pyelocystitis and recurrent pyelocystitis?

Residual Foci of Infection in the Genito-Urinary Tract.

It is of fundamental importance in treatment to determine the reason for persistence of infection. Residual foci of infection may persist in the urinary tract itself. Too often patients are examined who give a long history of chronic pyelitis or recurrent urinary infection and who have never had any investigation. Such patients should have at least a radiological examination and a microscopic examination of the urine with attempts at culture. Often the patient is found to have urinary calculi, infected hydronephrosis or even pyonephrosis.

As an example, I recently examined a nurse, aged nineteen years, who gave a history of eleven attacks of right-sided pyelitis in eight years, and who had had no previous investigation. She was found to have a *Bacillus coli communis* infection of the right kidney, which contained a large staghorn calculus.

If no obvious cause can be found in the urinary tract, then foci of infection should be looked for in the genital tract. In the male recurring pyelocystitis is sometimes associated with a prostato-vesiculitis, and treatment of the latter eliminates the recurrent urinary infection. In the female, urological investigation often gives negative results, and gynæcological examination is advisable. Often cervicitis with the accompanying discharge is the reason for reinfection of the urinary tract. The finding of persistent sterile pyuria in a young adult with bladder symptoms should always lead one to suspect a tuberculous condition. Another possible cause is the condition known as amicrobic pyuria or abacterial cystitis, which responds well to arsenicals. Persistent sterile pyuria also sometimes occurs with renal calculi, which act as irritants to the renal pelvic mucosa.

Obstruction.

The surgery of urinary infections is essentially the treatment of obstruction. Obstruction favours the persistence of and recurrence of infection. Medical forms of treatment are usually successful in the acute stages of infection, but recurrence can be expected if the underlying obstructive factor is not dealt with. One cannot expect to eliminate even a susceptible organism when obstruction to the urinary outflow exists. This has been stressed in the literature dealing with streptomycin, but also applies to therapy in general. Briefly, in children the commoner forms of obstruction are phimosis, *atresia meati*, and the presence of a urethra of congenitally small calibre. The forms of treatment are circumcision, meatotomy and urethral dilatation respectively. The less common forms of obstruction are congenital valves or transverse mucosal folds in the posterior part of the urethra or congenital median bar at the bladder neck, the treatment for which is transurethral diathermy or resection. In the adult female, obstruction in the lower part of the urinary tract may be due to a stricture (treated by dilatation), or to a median bar at the bladder neck, resection of which sometimes gives remarkable relief. In the adult male, urethral stricture and bladder neck obstruction in the form of median bar, adenoma or carcinoma are the chief obstructive factors. The treatment depends on the individual case. Minor degrees of bladder neck obstruction are important when vesical diverticula are present and in association with the bladder dysfunction due to *tabes dorsalis*. The resulting stasis and residual urine in the above conditions predispose the patient to chronicity of infection.

Foreign Bodies and Calculi.

Foreign bodies in the bladder and the presence of calculi in the urinary tract also favour the persistence of and recurrence of infection, in spite of chemotherapy and antibiotics. Foreign bodies should be removed. The treatment of the calculus depends on the individual case, and should include the factors responsible for formation of the calculus.

With streptomycin, successful control of infection can be anticipated only if urological treatment is undertaken prior to or in conjunction with the use of the drug.

Pyelonephritis.

Nephrectomy is rarely indicated for unilateral pyelonephritis. It is sometimes necessary to relieve pain. It is sometimes also indicated in pyelonephritis associated with hypertension. In January, 1948, Sabin[6] analysed the 100 cases reported in the literature of hypertension associated with unilateral renal disease, for which nephrectomy had been performed. The commonest pathological condition was unilateral pyelonephritis, occurring in 45% of cases, examination of the kidneys frequently revealing much atrophy. The results were as follows: (*a*) 26% of patients showed no relief of symptoms or hypertension; (*b*) 23% showed considerable symptomatic improvement and only a temporary fall in blood pressure; (*c*) the blood pressure of 51% returned to normal, but only half the patients had been followed up for more than a year.

The cases of hypertension which can be cured by nephrectomy are comparatively rare. A successful result following nephrectomy can be anticipated in the following circumstances: (i) when examination of the diseased kidney reveals chronic pyelonephritis and atrophy; (ii) when the healthy kidney is normal functionally, bacteriologically and radiographically, and in addition shows compensatory hypertrophy; (iii) when the patient is young; in children aged under ten years the results were excellent; (iv) when the hypertension is of short duration, as arteriosclerotic changes occurring in the sound kidney in hypertension of long standing diminish the chance of a successful cure by nephrectomy.

So in unilateral pyelonephritis with hypertension a thorough investigation and assessment are necessary before nephrectomy is decided on.

Calculous Disease and Urinary Infection.

Ureteral Calculus.

The combination of ureteral calculus and urinary infection often presents difficult problems. When dealing with a ureteral calculus and sterile urine, one can often treat the condition expectantly. However, when there is recurrent pyelonephritis with the usual rigors, "swinging" temperature and leucocytosis, the surgical indication is removal of the ureteric calculus even though it is small. The condition may even constitute a surgical emergency. It is justifiable to try endoscopic procedures to deal with small stones; but time should not be wasted in repeated endoscopic manipulation, especially in the presence of a severe infection in a toxæmic patient. As soon as calculus impaction occurs in association with infected urine, operative removal of the calculus is indicated, otherwise an infected hydronephrosis with pyelonephritis or a pyonephrosis develops, and so the ultimate destruction of the kidney results. This is all the more serious when the patient has bilateral renal disease or has already had one kidney removed. These remarks also apply to a calculus impacted at the uretero-pelvic junction with infected pelvic contents dammed up behind it. It should be understood that medical measures—chemotherapy and antibiotics—are employed in addition to surgery.

Renal Calculi.

The surgical removal of a calculus is but one phase of treatment, and one has not accomplished much if the important factors in stone formation and recurrence—namely, obstruction and urinary infection—have not been eliminated. The recurrence rate of secondary calculi—that is, those which have developed in association with urinary infection, particularly the urea-splitting organisms such as staphylococci and *Bacilli proteus*—has been given as 20% to 30% after treatment by conservative surgical measures such as nephrolithotomy and pyelolithotomy (Hyman[7]).

In the treatment of infected calculous kidneys, radical surgery—that is, nephrectomy—is indicated in the presence of a gross infection, particularly when the organisms are staphylococci or *Bacilli proteus*, as otherwise recurrence of calculus is almost inevitable. When conservative surgical measures are followed, involving removal of the calculus in less severe grades of infection, it is most important to attempt to eliminate any remaining infection or obstruction during convalescence. In such cases a follow-up is advisable so as to control the urinary infection which appears to play a dominant role in recurrence.

Infected Hydronephrosis.

Infected hydronephrosis is usually associated with obstruction in the ureter, commonly a calculus, or at the uretero-pelvic junction from a calculus, aberrant vessel or a band. The indications for nephrectomy are gross infection, toxicity and poor renal function. In the presence of good function and mild infection, one may adopt conservative measures, such as removal of the obstruction, and perhaps in addition a plastic procedure at the uretero-pelvic junction, combined with control of the infection by chemotherapy and antibiotics as indicated. Each case should be treated on its merits. Treatment is largely governed by the condition of the other kidney.

Pyonephrosis.

In pyonephrosis, if possible, a primary nephrectomy should be carried out. This will depend largely on the patient's general condition, on the size of the pyonephrosis, and on the severity of the infection. When the patient's condition will not permit a nephrectomy, then a preliminary nephrostomy is necessary. The secondary nephrectomy should be undertaken as soon as the patient appears to be in a condition to stand operation—usually within a month. Blood transfusion is often necessary during a secondary nephrectomy, and it pays to make arrangements for it in advance. A secondary nephrectomy is frequently a difficult and tedious operation owing to fibrous adhesions, and when possible a primary nephrectomy is preferable.

Renal Carbuncle.

Renal carbuncle is a localized subacute suppurative renal lesion of hæmatogenous origin. It is due to a staphylococcal infection and occurs in relation to furunculosis, osteomyelitis or carbuncle elsewhere. It is usually characterized by loin pain, rigors, sweating and loss of weight. Urinary symptoms are usually absent. The urine is usually free of pus and organisms, which may also be the case in the presence of closed pyonephrosis and perinephric abscess. Positive findings are loin tenderness, pyrexia, leucocytosis and sometimes a pressure deformity of a calyceal outline or splaying apart of adjacent calyces in the excretion urogram. An associated perinephric abscess sometimes occurs. Treatment is conservative, and the condition usually responds well to chemotherapy and penicillin. With healing, the pyelographic changes gradually revert to normal.

Perinephric Abscess.

Perinephric abscess may be of renal or hæmatogenous origin. The urine is frequently sterile and free of pus. The condition responds well to chemotherapy and the administration of penicillin. In some instances, resolution would probably occur with these alone if they are instituted early enough. However, the old surgical aphorism, "where there is pus let it out", still holds good, and incision and drainage mean an early relief of symptoms and a shorter convalescence.

Alkaline Encrusted Cystitis and Ammoniacal Cystitis.

In alkaline encrusted cystitis and ammoniacal cystitis the urine is offensive and has an ammoniacal odour due

to the conversion of urea to ammonia by urea-splitting organisms, particularly *Bacilli proteus* and staphylococci. Usually a mixed infection is present. Deposition of phosphatic salts occurs on the inflamed bladder mucosa, and the condition is often associated with a neoplasm which becomes encrusted with phosphates. Ammoniacal cystitis is also sometimes found in prostatic patients in whom gross infection has developed.

It has been found impossible in the presence of an infection due to urea-splitting organisms to acidify the urine by the oral administration of acidifying agents or dietary means. Treatment consists primarily in the use locally of acid solutions. The introduction by Suby, Allbright and others of the solutions known as Suby "G" and Suby "M" has been a great advance. The composition of Suby "G" solution is as follows: citric acid monohydrate, 32·5 grammes; magnesium oxide anhydrous, 3·84 grammes; sodium carbonate anhydrous, 4·37 grammes; distilled water to 1000 millilitres.

The reaction of this solution is adjusted to give a pH of 4·0. The formula for Suby "M" solution is as for Suby "G" solution, except that the former contains twice the amount of anhydrous sodium carbonate (8·84 grammes). It is less acid and better tolerated than Suby "G" solution.

The ideal method of treatment is by continuous drip through a two-way catheter for a week or more, or alternatively, intermittent irrigation as necessary, depending on the intensity of the infection and degree of encrustation. In prostatic subjects with ammoniacal cystitis the urine improves very much with this treatment. It is advisable at the same time to acidify the whole urinary tract by oral administration of acidifying agents, as an alkaline condition of the upper part of the urinary tract will tend to frustrate local therapeutic measures to the lower part of the urinary tract. Other treatment consists in relief of the obstruction, removal or solution of calculi and the use of sulphonamide drugs and antibiotics as indicated.

Chronic Interstitial Cystitis (Submucous Cystitis, Hunner's Cystitis).

The symptoms of chronic interstitial cystitis are typical—frequency of micturition, "trigger pain" on vesical distension to a certain point, sometimes suprapubic pain and mild hæmaturia. The urine is free of pus and sterile. A submucous and interstitial infection is present with resulting interstitial fibrosis. The vesical capacity becomes progressively reduced owing to the interstitial fibrosis and vesical hypertonicity. Cystoscopic findings are typical—an area or areas of congestion, usually on the posterior wall or fundus, which bleed readily when the bladder is distended beyond a certain point. Investigation of the upper part of the urinary tract gives negative results. Local treatment consists in the use of instillations of increasing concentrations of silver nitrate, hydrostatic dilatation under anæsthesia, and transurethral diathermy to the affected areas. General treatment includes the use of arsenic and hormones with variable results.

In those cases in which the vesical contracture is considerable and the frequency of micturition is half-hourly, uretero-sigmoidostomy is worthy of consideration to provide symptomatic relief.

Fistulæ.

When infection of the urinary tract is a result of fistulæ connecting the alimentary and urinary tracts, then the fundamental factor in treatment is cure of the fistulæ. The commonest fistula is vesico-colic fistula due either to diverticulitis or to carcinoma. The first step in treatment is diversion of the bowel contents by a colostomy and then medical treatment of the urinary infection. Later it may be possible to cure the fistula by dissecting the bowel off the bladder.

Conclusion.

The surgical treatment of urinary infections is essentially the treatment of obstruction. Medical and surgical treatment go hand in hand, and an understanding of the underlying factors is essential in order to obtain successful results.

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OBSERVATIONS ON THE EFFECT OF HIGH FAT DIET IN ALLOXAN DIABETIC RATS.

By J. BORNSTEIN[1] and J. F. NELSON,

From the Baker Medical Research Institute, Alfred Hospital, Melbourne.

IT has been shown that diets rich in fat ameliorate the diabetic state produced by the injection of anterior pituitary extract into dogs.(1) Burns and his associates(2) noticed a similar phenomenon with the diabetes produced by the subcutaneous injection of alloxan into rats. In contrast to the diabetes in Burns's experiments, which was rarely fatal even though untreated, we found that diabetes produced by the intravenous injection of alloxan in doses varying from 40 to 60 milligrammes per kilogram was frequently very severe and in most cases resulted in death from ketosis in from five to twelve days (Table I). Accordingly it was considered worth while to repeat and extend this work, and so far as possible to investigate the nature of the mechanism involved.

Experimental Methods.

The ordinary standard diet of rats bred in this institute is a mixture of bread, bran, cabbage, lucerne, milk and added protein in the form of meat meal. As this was unsuitable for the addition of fat in the form of margarine enriched with vitamins, when desired, the animals were changed over to a mixture consisting of crushed oats (36%), maize meal (8%), bran (32%), pollard (16%) and meat meal (8%), to which fat was added by 20% increments to 60%, and finally to 70%.

In order to eliminate species difference, two strains of rats, albino and Wistar, were used.

Although there were differences in age, the animals chosen varied in weight from 125 to 265 grammes, the majority of them weighing about 200 grammes.

Diabetes was produced by the injection of alloxan monohydrate into a tail vein, in dosage varying from 40 to 60 milligrammes per kilogram. It was found that the severity of the diabetes did not necessarily correspond to the dose employed.

Male rats were used throughout, since it has been shown(3) that female rats are more prone to ketosis than males.

Of the eighteen rats employed for the purpose of fat feeding, twelve were rendered severely diabetic as judged by blood sugar estimations, degree of glycosuria and weight loss. The other six were only mildly diabetic as judged from the above-mentioned criteria.

The blood sugar content was determined by the Hagedorn-Jensen method. Blood was taken from the tail vein after six hours' fasting. The urinary glucose content was determined qualitatively with Benedict's solution. In the

[1] Working with a full-time grant from the National Health and Medical Research Council, Australia.

tables "+" indicates from a trace to about 1%, "++" from about 1% to about 2%, and "+++" over 2%. The urinary ketone content was detected by the Rothera test and Gerhardt reaction; "+" denotes Rothera "positive", Gerhardt "negative"; "++" denotes Rothera "strongly positive", Gerhardt "positive"; "+++" denotes Rothera "strongly positive", Gerhardt "strongly positive".

TABLE I.
Control Series I: Alloxan Diabetes, Normal Diet.

Date.	Weight.	Urinary Glucose.	Urinary Ketones.	Blood Sugar Level. (Milligrammes *per Centum.*)
Rat 1C:				
29.8.47	222[1]			
1.9.47	200	+++	0	382
3.9.47	200	+++	0	
5.9.47	195	+++	+	
8.9.47	187	+++	++	
9.9.47		Death		
Rat 2C:				
29.8.47	195[1]			
1.9.47	165	+++	+	385
3.9.47	155	+++	++	
5.9.47	142	+++	+++	
6.9.47		Death		
Rat 3C:				
29.8.47	147[1]			
1.9.47	137	+++	0	159
3.9.47	135	+++	Tr.	
5.9.47	134	+++	0	
9.9.47	135	+++	0	
16.9.47	132	++	0	
23.9.47[2]	134	++	0	
Rat 4C:				
29.8.47	218[1]			
1.9.47	185	+++	0	342
3.9.47	170	+++	0	
5.9.47	170	+++	+	
8.9.47	160	+++	++	
10.9.47	155	+++	+++	
		Death		
Rat 5C:				
29.8.47	175[1]			
1.9.47	152	+++	0	248
3.9.47	145	+++	++	
5.9.47	127	+++	+++	
6.9.47		Death		
Rat 6C:				
4.11.47	218[1]			
7.11.47	188	+++	0	140
9.11.47	185	+++	0	
11.11.47	180	++	0	
18.11.47	182	++	0	116
25.11.47[3]	190	+	0	
Rat 7C:				
4.11.47	200[1]			
7.11.47	183	+++	0	348
9.11.47	173	+++	++	
11.11.47	162	+++	+++	
13.11.47	145	+++	+++	
		Death		
Rat 8C:				
4.11.47	207[1]			
7.11.47	182	+++	0	236
9.11.47	178	++	0	
11.11.47	178	+	0	
18.11.47	185	+	0	
25.11.47[4]	185	++	0	
Rat 9C:				
4.11.47	126[1]			
7.11.47	113	+++	0	284
9.11.47	104	+++	0	
11.11.47	105	+++	+	
16.11.47	100	+++	++	
18.11.47	100	+++	+++	
		Death		

[1] Alloxan, 10 milligrammes, given intravenously.
[2] This animal remained quite healthy, although excreting considerable sugar, for two months and was then sacrificed.
[3] This animal remained in a state of good health for four more weeks, showing glycosuria throughout, and was then sacrificed.
[4] This animal lived for four weeks with constant glycosuria and was then sacrificed.

The eighteen rats were divided into three groups. In the first, eight rats (six severely diabetic and two mildly diabetic) were followed for seventy-three days. They were receiving diet rich in fat for fifty-two days and the stock diet for the last twenty-one days. In the second and third groups, animals then receiving a diet rich in fat were killed at various stages from twenty-two days to thirty-five days, and studies were carried out on the liver fat and liver glycogen contents.

TABLE II.[1]
Control Series II: Normal Animals on Fat-Rich Diet.

Date.	Weight.	Urinary Ketones.	Added Fat Diet.
Rat 10C:			
29.8.47	171		20%
1.9.47	165	0	40%
4.9.47	166	0	60%
8.9.47	168	0	70%
15.9.47	178	0	70%
22.9.47	176	0	70%
1.10.47	174	0	70%
8.10.47	178	0	70%
Rat 11C:			
29.8.47	175	0	20%
1.9.47	162	0	40%
4.9.47	168	0	60%
8.9.47	165	0	70%
15.9.47	173	0	70%
22.9.47	176	0	70%
1.10.47	178	0	70%
8.10.47	181	0	70%
Rat 12C:			
29.8.47	220	0	20%
1.9.47	200	0	40%
4.9.47	208	0	60%
8.9.47	215	0	70%
15.9.47	220	0	70%
22.9.47	218	0	70%
1.10.47	218	0	70%
8.10.47	221	0	70%
Rat 13C:			
29.8.47	175	0	20%
1.9.47	167	0	40%
4.9.47	174	0	60%
8.9.47	175	0	70%
15.9.47	176	0	70%
22.9.47	181	0	70%
1.10.47	178	0	70%
8.10.47	180	0	70%

[1] From this set of controls it may be seen that ketosis is not produced in normal animals by a fat-rich diet; the initial weight loss was due to the animals refusing to eat their changed diet, unlike the diabetic animals, with which there was very little difficulty in this way.

In addition to the above, four control groups were set up; in the first, nine animals were rendered diabetic by the foregoing method and left on the normal diet; in the second, four normal animals were fed on a diet rich in fat in order to determine its ketogenic effects. Under groups three and four studies were made of the liver glycogen content of severely diabetic animals receiving a stock diet and of normal animals receiving a diet rich in fat.

TABLE III.
Control Series III: Six Rats.[1]

Rat Number.	Glycogen Values.	Degree of Diabetes.
1	0·2%	Severe, ketosis present.
2	0·05%	Severe, ketosis present.
3	0·75%	Severe, ketosis present.
4	7·0%	Mild, glycosuria only.
5	0·7%	Severe, ketosis present.
6	0·2%	Severe, ketosis present.

[1] The liver fat content in all these animals ranged from 7·6% to 9·2%.

Results and Discussion.

In the first group of controls it was found that of the nine animals used, six died in from five to twelve days with severe ketosis; the other three, being mildly diabetic, survived for an indefinite period (Table I).

In the second group of normal controls it was found that after the rats had overcome their distaste for the diet, which made it necessary to increase the amount of fat by gradual increments, they thrived, and at no stage did ketosis develop (Table II).

In the third group of controls it was found that the liver glycogen level was low in severely diabetic animals showing a slight degree of ketosis, but only the mildly diabetic animal had a normal liver glycogen content (Table III).

In the fourth group of controls high liver fat values and glycogen values in the normal range were found (Table IV).

In group I of the experiments a similar pattern was observed in all instances. No animal died of ketosis, in spite of the fact that five of the six severely diabetic animals developed ketosis while receiving diets varying from 40% to 60% in fat content, the lower concentration being more ketogenic; but in all the ketosis cleared up when the added fat was raised to 70%.

In all animals of this group there was an initial fall in weight, the rate of which was lessened by the addition of 20% of fat. Then there was gain, or at least maintenance of weight, which was accompanied by a steady fall in the blood sugar level (see Table VI) until the animals had been receiving a 70% fat diet for ten days or diet rich in fat for twenty-four days. Then occurred a sharp fall in body weight accompanied by a transient rise in blood sugar level. At this stage one of the animals died, no obvious cause being found at autopsy. The weight loss continued, although the blood sugar levels fell to normal. When on the fifty-third day the animals were given the normal stock diet, the diabetes recrudesced, but in a much milder form, the animals gaining in weight despite higher blood

TABLE IV.

Control Series IV: Six Rats, Normals, Receiving Diet with 70% Added Fat.

Rat Number.	Liver Fat Level.	Liver Glycogen Level.
1	9·8%	5·0%
2	13·7%	2·0%
3	10·7%	2·0%
4	13·1%	3·5%
5	11·9%	5·5%
6	11·7%	3·1%

TABLE Va.

Observations on Urinary Output.

Control Series.	Blood Sugar Content. (Milligrammes *per Centum.*)	Urinary Output. (Millilitres in Twenty-four Hours.)
1	236	26
2	348	37
3	385	41
4	219	32
5	148	24

TABLE Vb.

Observations on Urinary Output.

Experimental Series.	Added Fat Diet.	Blood Sugar Content. (Milligrammes *per Centum.*)	Urinary Output. (Millilitres in Twenty-four Hours.)
Rat 2	40%	343	8
	70%	160	6
	Nil	153	22
Rat 5	40%	134	6
	70%	95	6
	Nil	175	28
Rat 7	40%	370	7
	70%	146	5
	Nil	250	32
Rat 9	40%	348	8
	70%	214	6
Rat 17	40%	148	4
	70%	110	6
Rat 15	40%	252	8
	70%	186	6

TABLE VI.

Analysis of Figures in Phase I.[1]

Days.	Added Fat Diet.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
1		165	Nil	Nil	118
	Alloxan, 1	0 milligrammes, intravenously.			
3	20%	151	100% +++	Nil	268
			75% +++		
5	20%	152	12·5% ++		
			12·5% +	Nil	
10	40%	155	75% +++	12·5% +++	291
			12·5% ++	12·5% ++	
			12·5% +	25% +	
17	60%	150	12·5% +++	25% +	228
			50% ++		
			25% +		
			12·5% 0		
24	70%	149	0 +++	Nil	165
			12·5% ++		
			37·5% +		
			50% 0		
31	70%	137	0 +++	Nil	189
			25% ++		
			63% +		
			12% 0		
36	70%	136	30% +++	Nil	239
			14% ++		
			14% +		
			42% 0		
45	70%	123	33% +	Nil	161
			67% 0		
52	70%	119	Nil	Nil	129
59	Nil[2]	135	16% +++	Nil	205
			68% ++		
			16% +		
66	Nil[2]	140	16% +++	Nil	182
			68% ++		
			16% +		
73	Nil[2]	145	33% +++	Nil	174
			50% ++		
			16% +		

[1] The only group followed right through; two mildly diabetic, six severely diabetic.
[2] Normal diet.

TABLE VII.[1]

Experimental Series: Six Rats, Alloxan Diabetic, Condition Partly Controlled by Diet with 70% Added Fat; Liver Fat and Glycogen Values.

Rat Number.	Degree of Diabetes.	Blood Sugar Content. (Milligrammes *per Centum.*)		Liver Fat Content.	Liver Glycogen Content.
		Initial.	When Killed.		
9[2]	Severe.	348	189	9·7%	3·4%
10	Mild.	150	194	15·3%	5·2%
11	Mild.	148	189	13·0%	6·0%
12[2]	Severe.	310	316	9·1%	3·6%
13	Mild.	166	123	12·6%	5·4%
14	Moderate.	215	166	10·8%	6·1%

[1] All the above rats were killed while weight loss was occurring.
[2] Ketosis while receiving diet with 40% to 60% added fat.

sugar levels and pronounced glycosuria. After three weeks' further observation the animals had to be sacrificed, owing to the development of tail infections as a result of the repeated taking of blood from the tail veins.

During the first stage of the experiment it was noted that the earliest effect of the diets rich in fat was sharp diminution in urinary output, even at a stage when the blood sugar level remained high. The output became high again when the animals were returned to a stock diet. This was confirmed during the later stage, particularly in the case of one animal (Example 6), in which there was no diminution in the blood sugar level at any time. The results of these experiments are summarized in Tables V and VI.

As it was thought that the weight loss might be due to vitamin deficiency and/or to lack of high-grade protein, these were added to the diet of the second group; but the animals followed exactly the same pattern in respect to body weight as in the previous group.

From the above results we can partly corroborate the findings of Burns[3] and of A. Lazaris and T. G. Ugodnikova, as recently summarized in *Chemical Abstracts*.[4] Unfortunately the latter article is not available. The principal difference is the great weight loss which occurred in all our animals from the twenty-fourth day onwards, accompanied by a transient rise in blood sugar level. This differs entirely from Burns's findings; but Lazaris and Ugodnikova kept their animals on the high fat diets for only sixteen days, and this may account for the difference. We are unable to account for this phenomenon, although the rise in blood sugar level may possibly be due to glyconeogenesis.

TABLE VIII.[1]

Experimental Series: Four Rats, Killed while Weight was being Maintained on Diet with 70% Added Fat.

Rat Number.	Degree of Diabetes.	Blood Sugar Content. (Milligrammes *per Centum*.) Initial.	When Killed.	Liver Fat Content.	Liver Glycogen Content.
15	Severe.	361	186	9·4%	4·0%
16	Severe.	385	184	9·8%	3·5%
17	Severe.	355	188	11·3%	5·0%
18	Severe.	385	212	9·7%	4·2%

[1] All rats showed ketosis when receiving a diet with 40% to 60% added fat.

TABLE IX.

Analysis of Effect of Diet Rich in Fat on Twelve Severely Diabetic Animals.

Days.	Added Fat Diet.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum*.)
1		182	Alloxan, 10 mi	lligrammes, intr	avenously.
3	20%	167	100% +++	8% +	333
5	20%	165	100% +++	16% +	
10	40%	168	100% +++	8% +++ 42% ++ 33% + 17% 0	323
17	60%	168	33% +++ 50% ++ 17% +	8% ++ 16% + 76% 0	259
24[1]	70%	166	8% +++ 33% ++ 33% + 25% 0	Nil	207

[1] At this stage four animals were sacrificed for liver fat and glycogen estimations; the other eight animals followed the general pattern of sharp weight loss with reactionary rise in blood sugar followed by fall to normal levels, as shown in Table I.

The great diminution in urinary output confirms in all respects the findings of Lazaris and Ugodnikova, and is regarded as due to the direct action of fat, being completely independent of the blood sugar. The effect is apparently not renal, as histological study of the kidneys revealed no abnormality. At the moment we are unable to offer a satisfactory explanation.

The second group of animals consisted of two severely diabetic and four mildly diabetic rats. These animals with one exception (Example 6), in which the blood sugar level remained high throughout, followed the identical pattern of the first phase. These animals were sacrificed after thirty-eight days, and the liver fat and glycogen contents were estimated. High liver fat and normal liver glycogen values were found (Table VII).

In order to eliminate the possibility that the liver glycogen had been laid down as a result of the breakdown

TABLE X.

Effect of Diet Rich in Fat on Mild Alloxan Diabetes (Six Animals).

Days.	Added Fat Diet.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum*.)
1		208	Alloxan, 10 mil	ligrammes, intr	avenously.
3	20%	198	50% +++ 50% ++	Nil	161
5	20%	194	17% +++ 50% ++ 33% +	Nil	
10	40%	197	17% ++ 66% + 17% 0	Nil	125
17	60%	194	67% + 33% 0	Nil	134
24[1]	70%	189	17% ++ 83% 0	Nil	132

[1] From this stage the animals in this group showed a marked loss of weight and a reactionary rise in blood sugar level, and followed the pattern shown in Table I. Comparison of Tables II and III shows that weight loss commenced earlier in the mildly diabetic group receiving a diet rich in fat than it did in the severely diabetic group.

TABLE XI.

Example I: Rat II.[1]

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum*.)
30.7.47	163	Alloxan mo	nohydrate, 1	0 milli-
4.8.47	148	grammes, +++	intravenousl 0	y. 235
		Commenced	20% fat diet.	
6.8.47	153	+++	0	
7.8.47	153	+++	0	
		To 40% fat	diet.	
11.8.47	160	++	0	343
		To 60% fat	diet.	
18.8.47	153	+	0	204
		To 70% fat	diet.	
25.8.47	147	0	0	160
1.9.47	133	+	0	202
8.9.47	127	0	0	157
15.9.47	122	0	0	148
22.9.47	116	0	0	139
		Returned to	normal diet.	
29.9.47	140	++	0	150
6.10.47	150	++	0	153
13.10.47	159	+++	0	181

[1] This animal had moderately severe diabetes which was gradually controlled by the fat-rich diet. After three weeks, however, the weight began to fall rapidly; there was first a rise in the blood sugar level and then a fall; on return to normal diet weight was gained rapidly although there was a recrudescence of the diabetic state.

of body tissues, four more animals, all severely diabetic, were given a diet rich in fat and sacrificed at the twenty-first day when weight was still maintained. The animals to this point had followed the general pattern described in group I, the weight being maintained and the blood sugar falling towards normal values. Again the liver fat content was high and the liver glycogen content was in the normal range (Table VIII).

TABLE XII.
Example II: Rat III.[1]

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
30.7.47	155	Alloxan, 10 milligrammes intravenously.		
4.8.47	140	+++	0	276
7.8.47	137	To 20% fat diet. +++	0	
11.8.47	136	To 40% fat diet. +++	++	343
18.8.47	130	To 60% fat diet. ++	0	338
25.8.47	129	To 70% fat diet. +	0	205
1.9.47	106[2]			

[1] The diabetes in this animal was severe, as shown by blood sugar levels; while it was receiving a 40% fat diet ketosis developed, but this disappeared when the fat content of the diet was raised to 60%. After three weeks of fat-rich diets, and two weeks of very fat-rich diets, the animal lost weight extremely and died.
[2] Death.

TABLE XIII.
Example III: Rat V.[1]

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
30.7.47	175	Alloxan, 10 milligrammes intravenously.		
4.8.47	168	+++		148
7.8.48	165	To 20% fat diet. ++	0	
11.8.47	162	To 40% fat diet. ++	0	134
18.8.47	165	To 60% fat diet. 0	0	132
25.8.47	161	To 70% fat diet. 0	0	95
1.9.47	152	+	0	200
8.9.47	144	0	0	164
15.9.47	131	0	0	152
22.9.47	131	0	0	119
		Back to normal diet.		
29.9.47	150	++	0	175
6.10.47	152	++	0	132
13.10.47	165	++	0	141

[1] The diabetes in this animal was mild. However, the blood sugar level fell when the fat in the diet was increased, but again the phenomenon of a rapid fall in weight with an initial rise in blood sugar level after three weeks is seen. The diabetes recurred after return to normal diet, but the animal's weight rose.

These glycogen studies show that diabetic rats, regardless of the severity of the diabetes, are capable of utilizing fat and laying down glycogen, whereas severely diabetic animals, although supplied with unlimited carbohydrate, are unable to do so. There appears also to be an inverse relationship between glycogen deposition and ketone body formation. As the carbohydrate content of the 70% fat diet is very low (about 17%), it is considered, in agreement with other workers, that these animals (both normal and diabetic) are capable of utilizing the breakdown products of fat metabolism for the purpose of laying down glycogen.

Lastly, it was decided to analyse the effect of the diet on (*a*) the severely diabetic group (twelve animals) and (*b*) the mildly diabetic group (six animals). The analysis is carried out only to the twenty-fourth day, because after this all animals lost weight, and also because animals at this stage were sacrificed for purposes of liver fat and glycogen estimations.

TABLE XIV.
Example IV: Rat VII.[1]

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
30.7.47	170	Alloxan, 10 milligrammes intravenously.		
4.8.47	138	+++	0	410
7.8.47	145	To 20% fat diet. +++	0	
11.8.47	145	To 40% fat diet. +++	+	370
18.8.47	138	To 60% fat diet. ++	0	193
25.8.47	136	To 70% fat diet. Trace	0	146
1.9.47	122	+	0	159
8.9.47	121	+++	0	314
15.9.47	118	+	0	168
22.9.47	115	0	0	145
		To normal diet.		
29.9.47	124	++	0	184
6.10.47	128	++	0	250
13.10.47	123	++	0	189

[1] This animal was the most severely diabetic of the first series, as shown by blood sugar level and marked initial weight loss. However, it followed the same pattern of ketosis, fall in blood sugar level, loss of weight accompanied by transient rise in blood sugar level, and recrudescence of diabetes on normal diet. The gain of weight on return to normal diet in this case was not pronounced.

TABLE XV.
Example V: Rat XVI.

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
15.1.48	165	Alloxan, 11 milligrammes intravenously.		
17.1.48	151	+++	0	385
19.1.48	148	To 20% fat diet. +++	0	
24.1.48	154	To 40% fat diet. +++	++	255
31.1.48	157	To 60% fat diet. +	0	186
7.2.48[1]	153	To 70% fat diet. +	0	184

[1] Sacrificed for liver fat and glycogen estimations—liver fat 9·8%, liver glycogen 3·5%. This animal followed the usual pattern for severely diabetic animals. The glycogen level is in the normal range.

The two groups show some significant differences. In the severely diabetic group ten animals showed ketosis on a 40% fat diet and three animals on a 60% fat diet, although the blood sugar level fell steadily and weight was maintained (Table IX).

In the mildly diabetic group, none of the animals developed ketosis at any stage, the blood sugar level fell initially, then remained steady, but there was a steady loss of weight from the time the animals were given a 60% fat diet (Table X).

From these results it is seen that severely diabetic animals appear to be able to utilize fat more readily than mildly diabetic rats, and this at present cannot be

accounted for; neither can the apparently permanent amelioration noted in group I.

It also appears from these results that in severely diabetic animals, diets containing 40% to 60% of added fat are ketogenic, and that the increase of the fat content to 70% abolishes the ketosis. This is of interest in view of the finding of Petren[6] in the use of diets rich in fat in human diabetes.

TABLE XVI.
Example VI: Rat LXII.

Date.	Weight. (Grammes.)	Urinary Glucose.	Urinary Ketones.	Blood Sugar Content. (Milligrammes *per Centum.*)
1.11.47	221	Alloxan, 11	milligrammes.	
3.11.47	208	+++	0	310
5.11.47	192	To 20% fat +++	diet. 0	
10.11.47	200	To 40% fat +++	diet. +	388
17.11.47	207	To 60% fat +++	diet. ++	321
		To 70% fat	diet.	
24.11.47	198	+++	0	319
1.12.47	192	+++	0	306
8.12.47[1] ..	195	+++	0	316

[1] Sacrificed for liver fat and glycogen estimation—liver fat 9·1%, liver glycogen 3·6%. This animal, severely diabetic as shown by blood sugar levels and marked early weight loss, differs from the general pattern rather considerably, as it is the only one in the entire series whose blood sugar level was not controlled by the fat-rich diet, whose ketosis persisted until several days of the highest fat diet had been given, and in whom very sharp and progressive weight loss did not occur after three weeks of a fat-rich diet.

Summary and Conclusions.

1. A diet rich in fat ameliorates alloxan diabetes in rats, whether the diabetic state is severe or mild, and, if given for long enough periods, results in a permanent amelioration of the condition.

2. The weight is maintained only for a limited period of time, after which there is rapid weight loss accompanied by a transient rise in blood sugar level.

3. The urinary output is diminished by the direct action of the fat.

4. Severely diabetic animals are able to utilize fat more readily than mildly diabetic animals.

5. Of the fat-containing diets, a diet with 40% added fat is the most ketogenic in these animals, ketosis being abolished by elevation of the fat content to 70%.

6. Diabetic rats are able to utilize fat and convert it to glycogen, regardless of the severity of the diabetes. Severely diabetic animals receiving a high carbohydrate intake are unable to deposit glycogen; this suggests that glycogen is produced from the intermediate products of fat metabolism.

7. There appears to be an inverse relationship between glycogen deposition and the production of ketone bodies.

Further work on various aspects of the above findings is now in progress.

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DEAFNESS FOLLOWING MATERNAL RUBELLA.

By N. E. MURRAY,

From the Commonwealth Acoustic Laboratory, Commonwealth Department of Health, Sydney.

FOLLOWING reports by Gregg[1] of the relationship between maternal rubella during pregnancy and congenital eye defects in the children, and the publicity given to this work in Sydney,[2] it was found that other defects could also occur. These other additional defects were reported independently following investigations by Swan *et alii*.[3][4][5] In these reports and subsequent reports[6][7][8] increasing reference was made to cases of deafness, and others were also reported by Carruthers in Sydney.[9] Other references were also made to possible earlier cases[10] and to cases abroad, although in general the number of cases in overseas reports were small.

An investigation by a committee formed under the New South Wales Department of Public Health investigated medically many of the New South Wales cases.[11] This investigation tended to show that a large number of patients in New South Wales suffered congenital deafness.

The attention of this laboratory, then working under the auspices of the National Health and Medical Research Council on wartime deafness problems, was directed to this problem.

In order to study the possible social consequences of the rubella epidemic and to estimate the future educational and other special facilities necessary for these children, early and if possible accurate measurements of their hearing loss were desirable. The children were then about four years old.

Methods of Measurement.

Various methods of obtaining subjective and objective measurements of young children's hearing loss have been used.[12][13][14][15][16] In view of the almost complete absence of language in most of these children and the great use that could be made of accurate pure tone audiometric measurements of their hearing loss, special attention was directed to the obtaining of these measurements by means of a conditioned response first trained into the child.

During preliminary studies in November, 1944, it was found that provided sufficient time was available and in many cases the correct response used, in almost all cases when the children were aged four years or over an accurate audiogram could be obtained. The time and number of visits involved in obtaining the final audiogram varied considerably, mainly owing to the previous training and experience of children, many of whom were almost completely untrained socially.

It was necessary in most cases to carry out these audiometric measurements in such a way that the audiometer itself was not obvious, otherwise visual cues associated with the handling of the audiometer distracted the child from the simple response. Simple responses, such as the marking of a piece of paper on sound stimulus (for those used to drawing or crayon work), the moving of a finger or hand, and the pressing of a simple easily operated switch showing a flash of light were used. Later, to cover the great number of children and to provide for a number of visits when difficult children were to be tested, Mrs. Joyce Wark, a trained psychologist, joined the laboratory to assist in developing and extending the hearing tests.

A special room, located in a reasonably quiet position and given sound treatment, was decorated and laid out

in a kindergarten manner for this work. This assisted in winning the child's confidence and in making return visits enjoyable. Care was take to see that nothing in the way of a uniform or white coat was worn by laboratory personnel, as this might awaken fears and memories of previous visits to doctors, surgeries or hospitals for medical examination. With experience of more children it was found that the peg board provided a means of indicating a response which was suitable for most children. Placing a peg in the board in response to the sound often had the additional stimulus of providing a task to be completed—the fitting of all pegs—within the span of attention that could be given by the child, and in addition provided motivation, as the child is often pleased to show his ability to fill the board. In many cases, however, this desire to complete the task is so great that the child would complete the final holes without waiting for the signal. Often the child tends to anticipate the signal or thinks the response produces the signal. Sometimes the child's attention is focused on making patterns of the pegs.

The use of meaningful sounds to determine young children's hearing is discussed in detail in the literature, particularly by the Ewings.[13] These meaningful sounds are used in an attempt to explain or prevent apparent anomalous results observed in experimental work with young children. Meaningful sounds introduce some element

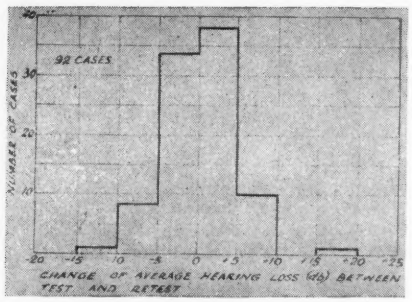

FIGURE I.

depending on the previous auditory experience of comprehension of the child apart from his degree of deafness. Such sounds may be considerably altered in their frequency spectrum, or amount of energy in the various frequency bands, at threshold, by the amount and type of hearing loss involved; thus erroneous conclusions may be drawn as to amount and type of deafness. Considerable subjective judgement and experience appear necessary; as these depend on the individual tester, results differ widely according to the experimenter.

If impact sounds are used, particularly those used to create loud noises, when almost total deafness is suspected, it is difficult to create these sounds at constant intensities on repetition. The ear responds at the threshold of discomfort, tickle and pain, largely in relation to the peak intensity of the sound; for impact or shock sounds this peak intensity may be twenty or more decibels above the average value, so that results may be responses to discomfort, tickle or pain thresholds and be meaningless, particularly if these thresholds are low.

We can obtain more consistent, reliable and easily comparable results from different testers where we finally use the pure tone audiograms as a measure of hearing loss, and also when we use, wherever necessary, preliminary meaningful sounds of various intensities or types with accompanying visual cues to assist in training into the child a conditioned response which may later be transferred to a similar response from a pure tone audiometer. In this way different subjective impressions of the different operators and variations in the children's knowledge of and response to meaningful sounds, which may vary considerably with hearing loss, are screened out of the final result. Considerable flexibility in the method of approach to different children or variations in technique from operator to operator are also possible.

By means of trained conditioned responses or "response activities" the children mentioned in this report have been tested by pure tone audiometers.

To assist in covering a large number of children quickly and to reduce the number of visits necessary, particularly for young or country children, much of the training in preliminary conditioned response can be done at home by the parents. For this work a scout whistle having root mean square value of 108 decibels or 120 decibels peak sound pressure is often used.

For very deaf children care has to be exercised in preliminary conditioning work, as means have to be employed in which the actual peak values of the sound are known. For these patients we use a pure tone audiometer with an extended range, which allows us to approach discomfort, tickle and pain thresholds with full knowledge of peak values of the sounds used. Possibly because of the greater

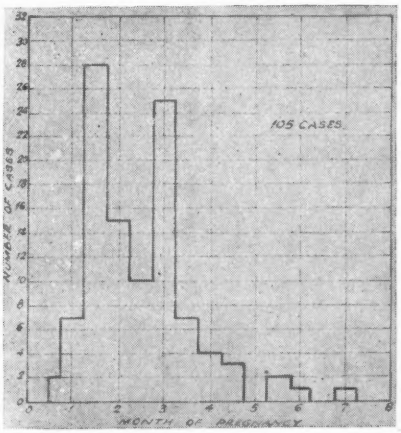

FIGURE II.

loudness steps for the same intensity changes due to recruitment of loudness in the nerve-deafened ears (at very high losses nerve deafness of some degree is always present), good responses and measurements can be obtained from these severely deaf patients.

For simplification, when making pure tone audiograms of young children the response is indicated only when the signal is heard to come on—it is switched on for a short time only; very short periods should not be used.[17] All measurements taken proceed from a conditioned response at a point somewhat above threshold down to threshold—that is, from "heard" to "not heard"; 1000 cycles are taken first, then 2000, 4000, 500 and 250. Additional frequencies or half-octave measurements are taken when this additional information would be useful.

Altogether a total of about 320 possible rubella-deaf subjects have been measured audiographically, distributed approximately as follows: New South Wales 150, Western Australia 70, Victoria 60, South Australia 40. All patients have not yet been covered. In an attempt to analyse closely these results, it has been found that the maximum significant data on deafness caused by rubella only could be obtained from the large New South Wales group, whose deafness was brought about by the 1940-1941 epidemic. Here close control could be obtained with regard to the certainty and time of the occurrence of the rubella. In some States, although thorough data were obtained with regard to rubella in the mother during pregnancy, no record was kept of subsequent childhood diseases that might also have caused some additional deafness. When cases in which there was a possibility of other contributing causes during early childhood and also all doubtful cases were excluded, we were left with a group of 105 cases for detailed analysis later in this paper.

The main effort in this measurement work at the present time is being directed towards extending these measurements to younger children aged about three or four years, and towards attempting to correlate partial measurements from younger children in the two to three years age group with later more accurate measurements, so that when possible the future course of educational treatment can be determined at the earliest required age, and hearing aids can be used if measurements indicate that they would be of assistance; an analysis of factors determining the earliest desirable age and measurements possible at that age is to be given in a later paper.

The pure tone audiograms initially made for these children at four years and in some cases at three years proved reliable on test and retest. However, opinions are expressed in the literature that pure tone measurements at this age are unsatisfactory. For example, Kerridge[16] states that rarely can children of six years of age be accurately tested with a pure tone audiometer and only

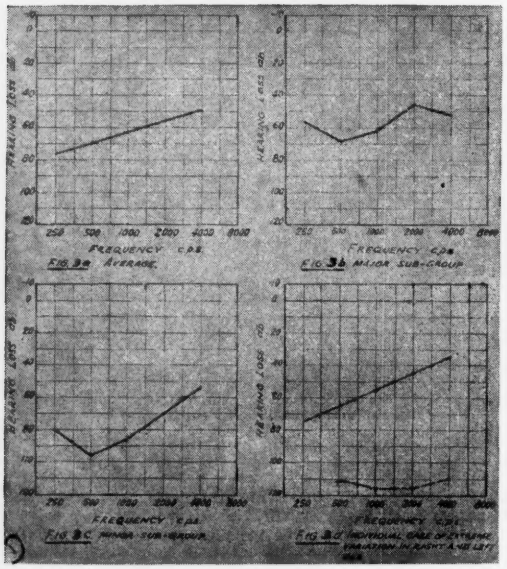

FIGURE III.
Typical audiograms.

the more intelligent seven-year-old children can be so tested. The Ewings[13] state that pure tone audiograms are unsatisfactory, and that the threshold reading is not obtained when children up to five years old are tested; recently the Ewings[23] state that they consider pure tones unsuitable for children aged less than six years.

In order to be certain that the measurements were being made at the threshold of hearing, a further series of tests was made on 92 children at four years old and nine months later at four years and nine months. It was thought that any tendency to respond to the threshold more accurately when the children became older would result in a lowering of the threshold at the second measurement, and that this latter series would on the average indicate that the children were less deaf than the former test. Figure I shows the result of these tests; the distribution of average hearing loss on test and retest is almost all within $\pm 5{\cdot}0$ decibels and is evenly distributed about the original measurement; a few measurements shown well outside this range appear to be due to real differences in deafness at the two times. Our measurements give an indication of hearing loss comparable in accuracy with that obtained in clinical audiometry with adults. The full results were first announced in a paper which I read to the Oto-Rhino-Laryngological Society of New South Wales on March 20, 1947.

More recently independent confirmation that young children of this age can be trained to respond to pure tone thresholds has appeared (Dix and Hallpike[25]). Special apparatus, the peep-show, gives a single reading of the binaural loss from a loudspeaker over a smaller range of loss than a clinical audiometer; more detailed information is generally desirable.

For our purposes we required separate measurements from each ear over a range extending beyond the clinical audiometer limits to those limited by pain thresholds. Later the measurements of degrees and types of deafness in the less affected ear were made the basis of a system of classifying rubella-deaf and other deaf children in the pre-school age and of educating them according to the hearing obtained when they were fitted with a wearable hearing aid individually prescribed, adjusted and fitted from the child's audiogram. This work is described in other papers.[34][36]

Audiometer Calibration.

For some initial measurements commercial type audiometers were used; later it was found that maximum output was often insufficient for training response into the deafer

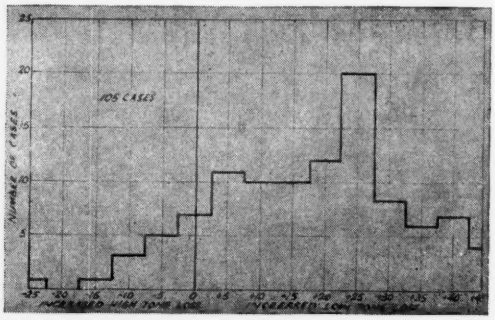

FIGURE IV.
Type of hearing loss. Change (decibels) over from octaves 250 to 4000 cycles per second.

children, and amplifiers to allow a safe extension were provided. Later still, special audiometers were built and calibrated with an extended intensity range for this work.

Calibrations of commercial type audiometers showed wide variations even when audiometers of the same make were used. This has also been found in another study.[33] When audiometers are used with the same earphone and earpad, precise relative objective acoustic calibrations can be made by means of the standard six millilitre artificial ear couplers with the 640 AA condenser microphone and sound pressure meter; absolute calibrations of the calibrating microphone are made by the reciprocity method.[18][19]

In the case of earphones and earpads in which the subjective measurements of threshold correspond closely with the objective calibrations, then objective calibrations can be made which correspond closely with subjective measurements.[20][21] In other cases the subjective calibration may differ considerably from the objective calibration in the standard six millilitre coupler and a correction is applied.

The actual output level at zero must also be known, so that the sound pressure level corresponding to the threshold for any degree of deafness can be determined. Reference is given[20][22] to normal threshold for an average of a very large number of ears; these articles include data from the United States of America Public Health Survey. This shows that the sound pressure level at normal hearing over a range most important to speech is approximately 20 decibels above 0·0002 dyne per square centimetre. This coresponds almost exactly with the American Standards Association specification setting. The measurements have been made with a W.E. 705A or "Permoflux" ANB-H-1A earphone calibrated to this standard.

Equivalent Hearing Loss for Speech or Average Hearing Loss.

In order to reduce our audiometric measurements to an equivalent hearing loss for speech, the average loss over the three octaves from 500 to 4000 cycles is used; first the mean loss within the octave is taken and then the average loss of the three octaves. This figure has been shown to be correlated closely with the hearing loss to speech in studies of temporary deafness (Davis *et alii*[24]) and to permanent deafness (Steinberg and Gardner,[22] Hughson and Thompson,[25] and Carhart[20]).

Experimental Data.

In a study of all patients tested, approximately 350 in all States, all cases were eliminated in which there was a doubt if the cause was due to rubella, in which there was some doubt as to when rubella occurred, and in which it was possible that childhood diseases might have

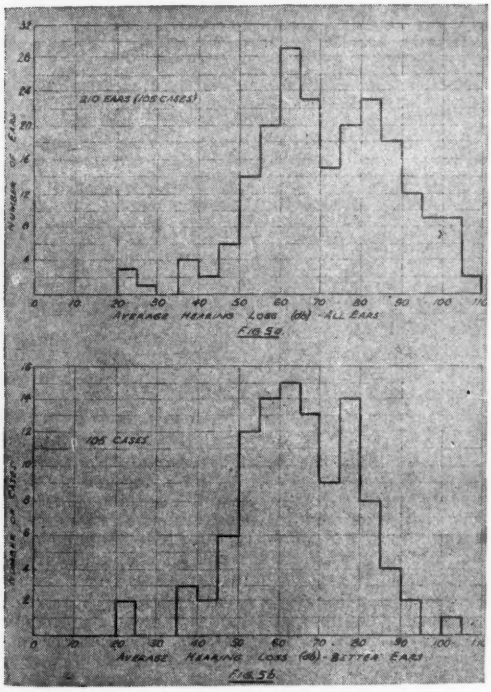

FIGURE V.
Distribution of average hearing loss (rubella).

had additional effects on hearing. This left 105 cases (210 ears) of the 1940-1941 group for analysis, the number of cases at each half-month of pregnancy being plotted on Figure II. This tends to indicate the occurrence of two peaks, one at six weeks' gestation and one at three months. These times correspond to major developments of the ear discussed by Mann,[27] the main development of the cochlea beginning at about six weeks, while the period at about three months corresponds closely with rapid development of the organ of Corti.[28] These two peaks would tend to make any average time suggested by Swan *et alii* rather meaningless. It would appear that deafness is more likely to occur if the mother contracts rubella at about the sixth week or the third month.

In an attempt to see if there is any relationship between the degree of deafness in the child and the time of occurrence of the disease during pregnancy, a study of deaf patients may give some clues to the study of other defects, as much better quantitative basis for study can be used for the deaf patients. The average hearing loss over the group at these two most frequent points (six weeks and three months) is interesting. The average hearing loss of these children, both ears being considered, is 72·1 decibels for those whose mothers contracted rubella at six weeks' gestation and 72·4 decibels at about three months' gestation, and the dispersion is similar. No tendency towards greater deafness appears to follow maternal rubella at either of these points. Where the number of patients with deafness resulting from rubella at any one period of the pregnancy is sufficient to give a reasonable sample, the mean of the individual average hearing losses appears independent of the time at which the disease was contracted.

It is possible to obtain further evidence on this point from the relationship between the decibel losses in any one child in the two ears. For the 105 cases the right ear-left ear correlation coefficient is 0·38, which is not highly significant. The wide difference noticed between two ears of the one child whose mother's rubella was definitely confined to one attack tends again to indicate little likelihood of a relationship between the degree of damage and the time of the rubella, differences as high as 56 decibels being found in the ears of one child (see Figure III(*d*)).

We may, therefore, conclude that the probability of the hearing's being affected appears much greater when rubella occurs at certain periods during pregnancy, but once the ear is affected the degree of damage appears independent of the time of occurrence of the rubella.

The general pattern of deafness is one in which the loss to low tones is greater than the loss to high tones, with a fairly even change throughout the speech range. Figure III(*a*) represents the mean of the 105 audiograms and may be considered the most typical or probable degree and type of loss. Figure III(*b*) shows a major subgroup of Figure III(*a*), which gives a sigmoid pattern, while Figure III(*c*), a minor subgroup, shows variations again in the subgroup shown in Figure III(*b*). Variations from an even change within the speech range greater than ten decibels are rare. Although elaborate classification of audiograms has been used in some cases (Carhart[20]), it does not appear warranted or necessary for our future management of these patients.

The hearing loss to speech depends on the individual average hearing loss, discussed earlier, and the type of hearing aid amplification required—frequency response—is substantially the same for all types of hearing loss.[30][31] Simple classification of our types of hearing loss is therefore sufficient. For analysing variations in types of hearing loss we have omitted minor variations in general type and have plotted the change in hearing loss over the four octaves 250 to 4000 cycles on Figure IV. As was mentioned earlier, the change is generally in the direction of increased low tone loss, although the reverse can occur in some cases. A wide distribution is seen with a most probable change of about 25 decibels' increased low tone loss in the speech range or about six decibels per octave.

In Figure V(*a*) the frequency of loss at various deafness levels for all ears is indicated; the mean loss is 72 decibels.

The hearing loss in the better ear is of major importance when possible future speech and language development and desirable educational techniques are considered, as well as in a study of secondary defects. The distribution of loss in the better ear is shown in Figure V, the mean loss being 65 decibels.

In this regard it appears somewhat harsh that the term deaf-mute has been used, when mutism is in almost all cases secondary to the primary deafness, and when in the majority of cases, if proper treatment is given, it should be of a temporary nature, varying from partial delay in developing normal speech to prolonged delay in development of defective speech.

Other secondary factors, depending largely on the residual hearing in the better ear, may be apparent lack of intelligence, general backwardness and behaviour difficulties resulting often from inability to communicate with the child and enforce discipline. This is often aggravated by a tendency to withdraw the child from normal social contacts, and often by lack of facilities for social contacts.

The deafness is seen to be generally from moderate to severe, but not total. The children as a group were

therefore particularly able to benefit from the use of hearing aids during their education and speech development, and the early accurate measurements of hearing loss made possible concentration on this aspect.[34] [36]

Summary.

Methods of estimating the hearing loss of pre-school children whose deafness was due to maternal rubella are discussed, and reasons are given favouring the desirability of obtaining pure tone measurements. Psychometric methods of obtaining the pure tone audiograms, initially by general visual and auditory cues which are later reduced to a single auditory pure tone response, are described.

Of approximately 350 cases measured audiometrically, 105 were considered as giving the most reliable data with regard to the time and certainty of occurrence of maternal rubella. Measurements in these 105 cases (210 ears) show that the probability of hearing loss is greatest when maternal rubella occurs at about six weeks or three months of pregnancy, corresponding to the development of the cochlea and of the organ of Corti respectively. Hearing loss is generally greatest in the low tones, decreasing on the average about six decibels per octave between 256 and 4096 cycles. Average hearing loss over the speech range in all ears is about 72 decibels, and for the better ears 65 decibels. Deafness is from moderate to severe but not total.

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THE OVER-EMPHASIS ON PSYCHIATRIC SYMPTOMS.[1]

By S. J. MINOGUE,
Sydney.

IN March, 1942, the Mental Hospital, Kenmore, New South Wales, was taken over by the army and its patients were transferred to other mental hospitals. Although a month's notice of the intended transfer was given, the time was almost dissipated in the futile attempts to keep the hospital as it was. In the end all hospital routine had to be sacrificed to get the patients away.

The evacuation caused a great emotional upset to staff and patients. The mental tension of members of the staff communicated itself to the patients, who then became so restless and unsettled mentally, that about fifty of them either escaped or asked for their discharge, which was granted in practically every case. Many of those transferred to other hospitals, not liking their new abode, improved mentally and were discharged. Few of those so discharged have since been readmitted to mental hospitals.

The patients concerned were mostly high-grade mental defectives or chronic delusional types, most of whom had been in the hospital for years. Whilst all of them were certifiably insane, subsequent events proved that they were capable of fending for themselves away from institutional care. The fact was that they had become institutionalized and were afraid to face life in the outside world. It was only when their fears of life away from hospital care had been overcome by a great emotional crisis that they became anxious for their discharge.

The results of this experience, which must be unique in the history of Australian mental hospitals, prove that there are many patients in mental hospitals who can safely be discharged. Even at the Mental Hospital, Rydalmere, where the patients are mostly senile, epileptics and mental defectives, all bad material from the point of view of this discussion, I found it possible to discharge

[1] Read at a meeting of the Australasian Association of Psychiatrists at Brisbane on June 8, 1948.

many patients, who had been in the hospital for years. But to do this it was essential to train the patients to think of their discharge rather than of their permanent detention, and to give them sufficient self-confidence to be able to stand on their own feet. To do this they had to be trusted more and more, and given more and more liberty. Jobs had to be secured for some; a few were allowed to go out to work by day and to return to the hospital at night, until they felt confident enough to leave the hospital permanently.

The higher grade mental defectives do improve amazingly in their mental condition when we trust them implicitly and throw greater responsibilities on to them. This practice is quite contrary to that taught in mental hospitals, where the sexual, thieving, lying and other tendencies of these patients are so stressed and feared that they are mostly kept under observation in closed wards, where no attempt is made to educate them or to unearth any talents they may possess. As they are punished for any misdemeanours by isolation in a single room or by a curtailment of their privileges, it is no wonder that they try to outwit everyone by the only weapons they possess, which are deceit and the striving for the good graces of the staff by the vicious habit of telling tales on their fellow patients. As a result many mental hospital wards are in a state of chronic tension because no patient trusts members of the staff or his fellow patients. Such discipline is that of a gaol and is not based on an understanding of the mental condition of patients.

If such patients can be given liberty and trusted more and more, we soon discover that they possess talents we least suspected in them. Their intelligence may be below the average, but the ability of many of them to do farm, labouring, routine factory and such like jobs is no whit inferior to that of many unskilled labourers in the outside world. Their deficiency is in the intellectual, not in the practical, sphere, and we simply allow our fondness for intelligence tests and our traditional mental hospital beliefs to blind us to their real talents. Many of these patients, once treated as mental defectives in mental hospitals, made excellent front-line soldiers in the second Australian Imperial Force.

Similarly a mental hospital training in the care of epileptics ignores almost completely their virtues, and confines itself to the precautions to be taken against the possibility of their injuring themselves. If they do happen to injure themselves the fear is always there that we may be held responsible. For far better is it to prevent one patient from injuring himself than to benefit 99 other patients, whose progress is being impeded by our precautions. Just as "the evil that men do lives after them, the good is oft interred with their bones", so, too, does one catastrophe in a mental hospital receive the full blast of unfavourable publicity, whilst all the good that that hospital does for its patients is forgotten. Who then is foolish enough to take risks in the treatment of patients? Thus has fear of unfavourable publicity destroyed in psychiatrists that spirit of adventure that built up our Empire and made English doctors pioneers in all branches of medicine, save psychiatry.

Truly is our training in the treatment of epileptics a purely negative one. We have never fully assimilated the lesson that many epileptics can lead normal lives, as indeed so many of our epileptic out-patients do. Surely we would do these patients greater justice if we learned to throw less emphasis on their vices and emphasized their virtues more.

Many mental patients can assume or discard their mental symptoms at will. Their mental condition has simply become a pose with them, to be discarded when anything better is offering.

One patient cut his throat and talked incoherent nonsense when he sought admission to a mental hospital. When I told him that it was unnecessary for him to go to all that trouble as I was prepared to admit him as a voluntary patient at any time, he told me that, if he did this, he would have to pay his own fare and he preferred the police to do it.

A patient who had chronic mania for many years suicided when told he had cancer of the stomach.

Another patient is the most incoherent and fantastically dressed patient I have ever known. Yet he can go to the races without escort, dressed and acting as a normal individual, without showing the slightest sign of any mental abnormality.

The truth seems to be that we are still being too influenced by the teachings of Kraepelin, and tend to think in terms of diseases rather than of patients, and of precautions to be taken in these diseases, rather than of their treatment and cure. We cannot think of melancholia, for example, without thinking of the suicidal tendencies of the patients; of primary dements without wondering how impulsive they may be; of paranoics without being afraid of their homicidal tendencies. Fears of what the patients may do paralyse our volition and keep us to a safe, unenterprising pathway, which experience has shown is safe for us, even though it is not always in the best interests of the patients.

We have fallen into the fundamental error in logic of basing our rules on exceptions and not on general principles, a common one amongst doctors today. Some melancholics suicide, we argue, therefore all of them will do the same unless we take special precautions to prevent it; as a few mental defectives have been guilty of sexual crimes, all of them must have the same tendencies; a few epileptics have been smothered by their use of soft pillows, so, therefore, all epileptics should use hard pillows. As accidents of all descriptions have happened to patients in mental hospitals over the years, and as so many rules and regulations have been devised to prevent their occurrence, the time has come when the welfare of patients and their treatment have become secondary to the administrative details deemed necessary for the safe running of these hospitals. In this way the initiative and independence of thought, so vitally essential for progress in psychiatric thought, have been stifled and almost killed by the adoption of safety-first principles, which have become an obsession in the administration of mental hospitals in the British Empire.

It may be that we, who are supposed to interpret human conduct and behaviour, have been unconsciously influenced by that craving for security, which has become part and parcel of our civilization. The fear of the future, the dread of making mistakes, the paralysis of volition engendered by the fear of what might happen—symptoms all so characteristic of an anxiety neurosis—are becoming more and more ingrained in our own characters.

In the course of his famous address to American psychiatrists in 1894, Weir Mitchell accused mental hospitals of neglecting the only thing that could give them vitality, which was research work. The address caused intense bitterness at the time; it was a criticism of bureaucratic control, which today has so extended that it is filching from us one by one our liberties. The effect of such control in mental hospitals, then as now, is that rules and regulations become of more importance than the welfare of patients; the letter of the law of far greater importance than its spirit; expediency of greater import than the general principles of medicine. Under such a *régime* mental hospitals have progressed but little and can progress but little in the future. Only those with a broad vision, unhampered by foolish traditions and precedents, can give them life and make them centres of learning and research work, well respected by the community. And let those who advocate the nationalization of hospitals study mental and other hospitals under government control for a century or more, and let them then ponder on the retrogression that must take place over the years in all hospitals under similar control. Then let them pray most devoutly: "From such a fate, dear Lord, deliver us."

After the outbreak of the last war, when the expansion of psychiatric knowledge became imperative, Australian army administrators mostly rejected psychiatry as practised in mental hospitals, and trained their own psychiatrists, who were not confused by outmoded teachings. *Orta recens quam pura nites.* The old terminology was resurrected and given new life. Schizophrenia, anxiety neurosis, obsessional neuroses and many others flashed across the screen with added brilliance.

Treatments, old and new—continuous narcosis, hypnosis, suggestion, occupational therapy, psychoanalysis and such like—were given new life. The newly discovered shock treatments became the vogue and were soon regarded as a panacea for all illnesses psychiatric. Symptoms of the neuroses were dissected more and more. A new science, somatic medicine, arose. Truly did it appear that the secrets of psychiatry had at last been unearthed and a new and brilliant science would sweep the world.

If we analyse the psychiatric literature of the war years we cannot but be struck by the ever-increasing emphasis on symptoms and not on diseases. Schizophrenia, for example, is no longer a definite disease, but a term loosely applied to any psychosis or psychotic symptom in a young person. Similarly anxiety neurosis includes all manner of neurotic symptoms, such as panic reactions, the effort syndrome and many others.

We tend to lose ourselves in a mass of words and to split straws. In this we are aided and abetted by psychologists, who, with their numerous tests, define individuals in terms of mathematical equations. Man is no longer a human being, with a body and a soul, but a carrier of psychiatric symptoms, which must be analysed, dissected and treated, oftentimes with no thought of how the treatment will affect him mentally or physically.

We now think that we can safely direct the life of any individual from the cradle to the grave. We never realize that from his infancy we are regimenting him and destroying any independence of thought he may develop in later life. As an infant he is fed by the clock, not when he himself wants to be fed. He is amused by expensive toys selected for him by adults. His school life is so planned that he must learn what we think he should learn and it is forbidden for him to develop his own talents in his own way. Corporal punishment is forbidden, even though a normal boy thinks nothing of corporal punishment, when it is a just punishment administered for the breaking of rules that he knew he should not have broken.

Perhaps we are too apt to think of children, not as children, but as adults who have enjoyed the same social status and experiences as we ourselves have enjoyed. Because we may have liked school, all children must like it. If a boy plays the truant he is a problem child and a juvenile delinquent. But the truth is that whilst most boys hate school, only those with initiative and independence of thought have the courage to express their disapproval in the only way possible for them. Others, with claustrophobia, find it psychologically impossible to stay in a closed class room. Thus it is that boys, born pioneers of Empire, are committed to reformatories because they have the courage to defy a regimented way of life that we think is in their best interests. Then, defiant because they have been so misunderstood, they go from bad to worse and become true criminals. We, as psychiatrists, can see only their delinquency. We blind ourselves to their great courage and initiative, which, properly developed, will lead them on to fame, perhaps fortune, in far-distant countries. When educationalists decide that all children must attend school until they are fifteen, there can be no exceptions, even though continued attendance at school will turn many of the children into neurotics or criminals.

We have a tendency to interpret life, not as it really is, but in the light of our own ideas. We seldom think that some of our present ideas may be wrong and will change with the passage of time. Thirty years ago "painted women" and prostitutes were synonymous terms; today the unpainted woman is a rarity. An immoral slum girl is a harlot; an immoral society lass "has a good time". A "scrounger" in the army, souvenir hunters in hotels, those who evade taxation, tram fares and other legal charges, are not stealing. They are simply doing what everyone else is doing. But the boy who steals fruit or money to pay his fare to a distant city, which he has an irresistible desire to see, is a delinquent child to be reformed at all costs. La Fontaine's fable of the lion and the ass is still true to life.

We must study man as a whole and see him with Pascal: "What a nightmare creature is man . . . a monster, a chaos, a mass of contradictions . . . judge of everything, yet a senseless worm; guardian of the truth, yet a cesspool of doubt and error; the glory and yet the off-scouring of the earth." From out of the mass of his contradictions we are apt to seize upon some psychiatric symptom and treat it energetically. How often, for example, do we see anxiety symptoms and not the man behind them? We are apt to forget that anxiety states may be diagnostic of physical illnesses, such as diabetes and heart disease. We even forget that most intelligent and imaginative persons become acutely anxious at times, as do many surgeons before an operation, barristers before entering a court, or famous sportsmen before entering the sports arena. Their anxiety has made them anticipate the course of events and be on the qui vive more than the average unanxious individual. They have learned to harness their anxiety and to divert its energy into useful hard work, which so often makes them famous.

Thus it is that psychiatric symptoms are not necessarily in themselves harmful. They may be symptoms of bodily ill health, or the expression of some mental disease, whose cause may be entirely unknown, or the manifestation of a person's sense of insecurity. They may even be manufactured as the result of malingering or of the extensive publicity given to the neuroses during the war years. In cases in which we suspect that psychiatric symptoms are secondary to bodily ill health it is surely our duty to minimize those symptoms, lest they should become fixed and permanent. In the true mental diseases we must not allow ourselves to be completely blinded by the psychotic symptoms present, but we should also endeavour to find out the capabilities of the patients, so that if we can develop them sufficiently the mental symptoms present will recede more and more into the background. If this policy was adopted to an intensive degree in mental hospital practice, the patient population of these hospitals would soon fall, and the need for new mental hospitals would be obviated.

One cannot doubt that the sense of insecurity, so prevalent in the community today, is a prolific cause of the neuroses. One by one the props that once gave us a sense of security are being taken away. The old family physician, the guide, philosopher and friend of his patients, no longer exists. He shared their sorrows and joys and helped them carry their burdens. He prescribed with dramatic success marriage for the thin, anæmic and nervous girl, who is now treated, without much success, by shock treatments and such like. Religion and patriotism, the only solaces for the masses, are now out of date. Their successor, psychology, puts a premium on materialism and worldly success, forgetful of the fact that most neurotics have an uncanny sense of reality and are able to see in their true light the artificialities of the world around them. It cannot offer them, as religion especially can, a true refuge for their fears and difficulties.

Divorce, too, has destroyed that sense of security a girl once sought in marriage. Contraception has made coitus a mere physical act, which takes no heed of the tremendous emotional and psychological tensions engendered by it. These tensions, instead of finding their normal outlet in children and their care, are perverted into anxiety symptoms, the bugbear of most married women who practise birth control. On the assumption that these anxiety symptoms are due to their mistrust of contraceptive technique, patients are fitted with cervical caps or sterilized by having their Fallopian tubes tied, without, as a rule, any relief of their symptoms.

Concentration on psychiatric symptoms has blinded us to the fact that history teaches that the road to happiness, so vainly sought by most neurotics, comes not from wealth or high position, but from hard work and the overcoming of trials and difficulties. Marriages tested by fire have always been the happiest. But our tendency today is to believe that the road to happiness lies in physical comforts and the avoidance of discomfort. At school short cuts to knowledge are preached. Labour-saving devices make life easier. We crowd into large cities (which have always in time destroyed previous civilizations) where life is easy and the discomforts of rural life are avoided. People are not allowed to think for themselves; diversions of all

kinds must be provided for them, even in hospitals. Initiative and the dignity of work have been lost sight of, and man, with too much time on his hands, turns his thoughts on to his own bodily symptoms, which keep on multiplying, despite all treatment.

During the war neurotic symptoms received so much publicity that many soldiers learned them off by heart and used them to secure their discharge from the army. One often wonders how many of the soldiers, who recovered dramatically after a few shock treatments, were malingerers. Others applied the symptoms to themselves, and like many medical students, convinced themselves that they were the victims of serious neurotic diseases. It is interesting to speculate in these cases to what extent the patients' answers to questions have been coloured by their knowledge of neurotic symptoms.

We have little to add to the teachings of the psychiatrists of old about the treatment of the true neuroses and psychoses. As to the vast majority of neurotics today, with their aches and pains, their fears and misgivings, we must recognize their need for someone to help them carry their burden of sorrow and give them hope and a refuge for the future. Oftentimes, because our imagination is unequal to the task, we will be unable to help them. Others are insincere and really do not want our help. But in all cases we are presented with a human being, with his weaknesses and his strength, his virtues and his vices, a human being who is tossed and turned and upset by the storms of life. To him we must throw a life-line, which he will grasp or reject. And in dealing with these patients we cannot do better than remember the prayer of members of Alcoholics Anonymous: "Oh, Lord! give us the courage to change the things we can change; serenity to accept those things we can't; and wisdom to know the difference."

SOME PROBLEMS CONCERNING THE ÆTIOLOGY OF RHEUMATIC FEVER.

By SYDNEY D. RUBBO,
Professor of Bacteriology, the University of Melbourne.

IT may be appropriate to commence this short discussion by stating that science is characterized by a continued search for more and more detailed explanation of ultimate causes. Once the term "miasma" served as an adequate designation of the cause of disease; then with the work of Pasteur, Koch and their students this vague term was replaced by the microbial theory of disease. Whilst it is sufficient to accept this theory for the majority of infectious disease processes, such an approach, when applied to rheumatic fever, yields but superficial information on the ætiology of this condition. The preoccupation in discovering a specific microbial cause for rheumatic fever which has characterized work in the past has, in my opinion, decelerated our understanding of its true nature.

Almost exactly twenty years ago the causation of rheumatic fever was discussed at a conference on rheumatic diseases held in Bath in 1928 with such conviction that the listeners must have been firmly convinced that the solution of this vexatious problem was at hand.[1] The passage of twenty years has failed to yield confirmation of many of the ideas expressed at this important gathering. This paper cannot be regarded as a complete statement of fact, but must be taken in some of its aspects with the proverbial grain of salt. Its aim, however, is to give form to current work on the subject and to stimulate discussion and research in Australia in this important field of medicine.

Any discussion concerning the ætiology of rheumatic fever must take into account the following factors: (i) the infectious element, (ii) the familial susceptibility, (iii) the age incidence, (iv) the tendency towards recurrence, (v) the histopathology of the disease, (vi) the clinical manifestations, (vii) the role of salicylates, (viii) the indifferent laboratory findings, (ix) the social distribution.

The Infectious Element.

The infectious element in rheumatic fever appears undoubtedly to be the Group A hæmolytic streptococcus, *Streptococcus pyogenes*. This statement is not based on the application of Koch's postulates, but on epidemiological data and the role of sulphonamides in reducing recurrency. It is quite definite that rheumatic fever, while endemic in any community harbouring hæmolytic streptococci, will increase during periods of streptococcal epidemics. This was well shown in the American Navy in World War II.[2] It is also worth noting that streptococcal infections are seldom seen in tropical regions and rheumatic fever is also a rare disease of these parts. Furthermore, we have definite evidence that the recurrence rate is significantly reduced by continuous prophylactic therapy with sulphonamide and that this measure also reduces the carrier rate of *Streptococcus pyogenes*.[3][4] These factors can leave no doubt of the importance of the Group A hæmolytic streptococcus, irrespective of its type, in precipitating a rheumatic attack.

Familial Susceptibility.

In regard to familial susceptibility the work of May Wilson[5] shows that rheumatic fever is an hereditary disease and the factors responsible for the susceptibility follow the general laws of a recessive Mendelian inheritance. For example, if both parents were rheumatic then every child would be susceptible to rheumatic fever; if one parent was rheumatic and the other a carrier (carrier signifies rheumatic fever in near relatives) each child would have a 50% chance to be susceptible. Whilst the familial susceptibility may be regarded as a necessary condition, it in itself is not a sufficient condition for the manifestation of rheumatic disease. Superimposed upon this familial susceptibility there is the infectious element, the Group A hæmolytic streptococcus, discussed above. If we accept these two factors as the necessary and sufficient conditions in the development of rheumatic fever, then an explanation is forthcoming for the relatively low incidence of rheumatic fever when compared with the widespread incidence of hæmolytic streptococcal infections. Hence, the seed and the soil determine the clinical outcome.

Age Incidence.

The age incidence, which we all know is greatest in children from four to fourteen years, reaching a maximum at the ages of six and ten years, is best explained in terms of exposure to the hæmolytic streptococcus either at home or at school. This exposure in its initial stages may give rise to sensitization in the genetically conditioned individual which manifests itself as a disease we call rheumatic fever. The susceptible individual, however, who escapes attack during adolescence may be regarded as one who, in spite of his or her exposure to streptococcal infection, has never reached the stage of sensitization recognizable at a clinical level. As age and exposure progress such an individual passes through the stage of silent sensitization to a state of desensitization, so that the chances of developing the disease in later life become progressively less. In short, we are postulating that not all individuals with the appropriate genetic background will necessarily develop clinically recognizable rheumatic fever following streptococcal infection. This argument is in accord with the well-known biological fact that susceptible individuals may harbour pathogenic organisms without complaining of disease at the clinical level.

Tendency towards Recurrence.

The tendency towards recurrence is entirely consistent with any views on the allergic basis of the disease. From the foregoing it is to be assumed that this allergy or hypersensitivity can arise only from single or repeated hæmolytic streptococcal infections in those individuals whose genetic background predisposes them to rheumatic fever. With increasing age this tendency to recur decreases, and this again is understandable as a process of natural desensitization.

The Histopathology of the Disease.

The histopathology of the disease undoubtedly shows that the lesions of aseptic inflammation, as characterized by the Aschoff nodule, are widespread throughout the body and distributed throughout connective tissues.[6] The lesions are in no way dissimilar from those produced during sensitization of an experimental animal to foreign protein.[7] Accordingly, the histopathology confirms the suggestion that we are dealing with a state of hypersensitivity or allergy, whichever term is preferred.

Clinical Manifestations.

The clinical manifestations, in the main, entirely reflect the distribution of the lesions of rheumatic fever. It is not infrequent that a history suggestive of recent streptococcal infection is elicited from the patient. The frequent absence of hæmolytic streptococci at the onset and the very low grade type of pyrexia appear to negate any suggestion that we are dealing with an actual infection. In fact, rheumatic fever is a misnomer in that it places far too much emphasis on the pyrexial element.

The Role of Salicylates.[8]

It is frequently said and with justification that polyarthritis in a child responding to salicylate therapy is pathognomonic of rheumatic fever. We are not at all clear how salicylates exert their beneficial effect not only in mitigating joint symptoms, but also in reducing tachycardia and lowering temperature. We can say quite definitely that salicylate is in no way antibacterial (maximum blood concentration is 35 milligrammes *per centum*) and it is improbable that salicylate is concerned with interference in the abnormal antigen-antibody reaction which I believe is operating. It has been suggested that salicylate interferes with the combination of the antigen with the antibody;[9] on the other hand, salicylate may indirectly reduce the toxicity of the antigen-antibody complex after it has been formed. This latter suggestion seems more appropriate, as salicylate therapy exerts its beneficial effect only when the patient is suffering from the results of this abnormal serological reaction. It is of no value prophylactically. A recent suggestion that sodium salicylate inhibits hyaluronidase activity cannot be seriously entertained.[10] In fact, this explanation must be completely abandoned in view of later work.[11]

The Indifferent Laboratory Findings.

The indifferent laboratory findings do not point one way or the other towards the specific ætiology of this disease. Hæmolytic streptococci may or may not be isolated at the onset of symptoms, the antistreptolysin titre may or may not be elevated at the onset of symptoms, the blood sedimentation rate is increased, but this is a non-specific phenomenon. The leucocytosis again can be interpreted as infectious or toxic. In general, the serological evidence (antistreptolysin titre) tends to confirm that the precipitating cause of rheumatic fever is recent infection by the hæmolytic streptococcus. It is noteworthy that this infection usually takes place about three weeks prior to the onset of the rheumatic fever incident. This time interval is reminiscent of the time interval required for the development of sensitization in animals experimentally injected with foreign proteins.

Social Distribution.

There is no doubt that rheumatic fever is less common among the well-to-do than among the working-class populations. Of the factors operating within the framework of poverty, damp houses and poor diet have often been suspect, but a more plausible factor associated with poverty seems to be the increased incidence of streptococcal infections among the lower income groups. Overcrowding with its attendant increased liability to droplet infection is probably one of the reasons why the incidence of rheumatic fever is heaviest in the poorer parts of our cities. This is supported by some recent work in Melbourne.[4] However, as the disease is not a notifiable one, it is impossible to analyse accurately its distribution throughout the community.

In summarizing the data already presented I feel we can be reasonably certain on two points, namely, that rheumatic fever may develop in a child following one or more hæmolytic streptococcal infections provided the genetic make-up of that individual predisposes him to susceptibility. The crucial point is the nature of the sensitizing antigen so produced. It is not in my opinion the proteins of the organism *per se*, nor is it the toxins (at least six) produced by the organism *in vitro*. It is probably a conjugate antigen, the integral parts being the streptococcus or one of its toxins and a connective tissue substance in the individual. The chemical combination of the organism and the tissue substance produces a new antigen distinct from either of the component parts. This antigen stimulates the production of antibodies (locally, in the tonsil, and systemically) which react specifically with the antigen or its haptenic group (the group determining the specific interaction between antigen and antibody). So long as this reaction takes place in the circulation no adverse effect is manifest, but reaction intracellularly or at cell surfaces will produce an acute inflammatory response. It is not improbable that the tissue component of the conjugate antigen acts as the haptenic group. If this assumption is correct it follows that the antibody so produced will react with tissue substances of the same chemical type wherever they may be found. On the basis of this argument the lesion which we recognize as the Aschoff nodule results from a combination of the circulating antibody (autoantibody in Cavelti's terminology) with the fixed tissue substance. This antigen-antibody reaction, if sufficiently pronounced, gives rise to a syndrome recognizable as rheumatic fever. An exactly analogous hypothesis can be stated for the genesis of nephritis; in this case the antibody is reacting specifically with renal tissue substance.[12] These suggestions are not without experimental support as evidenced by the recent work of Cavelti[13] and others.[14][15]

Conclusion.

The essential problem in the ætiology of rheumatic fever is the discovery of the antigen and its specific antibody. If we approach this subject along orthodox lines as laid down by Koch's postulates I feel that our progress will be checked. If, however, we succeed by less orthodox endeavours then it is not unlikely that laboratory tools will be placed at the disposal of clinicians which could be used in confirming the diagnosis in doubtful cases, in following the convalescence in established cases and in offering prognosis. Furthermore, it is anticipated that desensitization by immuno-prophylactic techniques might be available for those whose familial history suggests susceptibility.

One final point. The study of the ætiology of rheumatic fever extends beyond the laboratory approach described above. It is essential that the disease be made a notifiable one so that a fuller understanding of its geographical, urban, rural and domestic epidemiology will be accessible. The importance of this type of social inquiry has been recently stressed by Ryle.[16]

It is to be hoped that the public health authorities in Australia will follow the initiative of Norway, Denmark and Iceland by declaring rheumatic fever a notifiable disease.

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A HÆMAGGLUTINATION TEST FOR THE DIAGNOSIS OF INFLUENZAL MENINGITIS.

By M. F. WARBURTON and E. V. KEOGH,
Commonwealth Serum Laboratories, Parkville, Victoria,
AND
S. W. WILLIAMS,
Children's Hospital, Melbourne.

A PRESUMPTIVE DIAGNOSIS of influenzal meningitis is made on the observation of bacteria resembling *Hæmophilus influenzæ* in a specimen of cerebro-spinal fluid obtained from a patient with the signs and symptoms of meningeal infection. The diagnosis is confirmed by the positive identification of the organisms as *Hæmophilus influenzæ*, (i) after isolation, or (ii) by the production of capsular swelling by antiserum in hanging drop preparations of the cerebro-spinal fluid (Quellung test), or (iii) by demonstration of the specific capsular polysaccharide in the specimen by a precipitin test. The severity of the infection, and the response to therapy, may be assessed in the laboratory by measuring the content of reducing substances in the cerebro-spinal fluid (Alexander, 1939, 1942, 1943).

The diagnostic test described in this report is more sensitive than the precipitin reaction for detection of the specific polysaccharide of *Hæmophilus influenzæ* (type *b*) in the cerebro-spinal fluid. The test also gives a direct roughly quantitative measure of the concentration of polysaccharide, providing a means for assessment of the severity of the infection and the response to therapy.

The test is based on a recent observation that polysaccharides of many species of bacteria, including *Hæmophilus influenzæ*, are adsorbed from their solutions to the surfaces of red blood corpuscles. Erythrocytes so coated are agglutinated by serum containing antibody to the particular polysaccharide (Keogh, North and Warburton, 1947, 1948). The titre of an antiserum against erythrocytes coated with measured amounts of polysaccharide is determined by addition of such coated red cells to graded dilutions of the antiserum, note being made of the highest dilution of the antiserum in which the red corpuscles are agglutinated. If a little very dilute solution of polysaccharide is added to the dilutions of antiserum prior to the addition of the sensitized erythrocytes, the agglutinating titre of the serum is reduced, because the added polysaccharide combines with part of the antibody, rendering it unavailable for agglutination of the polysaccharide-coated erythrocytes. This phenomenon is illustrated in Table I, which records the titration of an antiserum (*Hæmophilus influenzæ*, type *b*) against erythrocytes sensitized with the capsular polysaccharide of that organism, the antiserum dilutions having first been mixed with graded dilutions of the polysaccharide.

It will be noted that the agglutination titre of the serum against the sensitized erythrocytes falls progressively after the addition of increasing amounts of polysaccharide. Two further points should be noted: first, that the addition of polysaccharide in a dilution of 1 in 10,000,000 is clearly detectable by a twofold reduction in the titre of the serum; secondly, that the relation between the reduction in serum titre and the amount of added polysaccharide is not a simple arithmetic proportion—in the experiment illustrated a thousand-fold increase in the amount of inhibiting polysaccharide effects approximately a thirty-two-fold decrease in the serum titre.

The set-up illustrated in Table I is clearly well adapted to the detection of minute amounts of specific bacterial polysaccharide in specimens of cerebro-spinal fluid, and it has proved so in practice. For maximum sensitivity, the reagents employed must be carefully standardized and adjusted. The methods for preparation of the bacterial polysaccharide, for optimal sensitization of erythrocytes and for titration of the antiserum are given below. It will be sufficient now to state that maximum sensitivity with freedom from false positive reactions is obtained by sensitizing the erythrocytes with minimal amounts of polysaccharide, and by reducing the concentration of erythrocytes in the final mixture to that minimum consistent with an unequivocal end point. The results of the examination of fifteen specimens of cerebro-spinal fluid obtained on admission to the Children's Hospital, Melbourne, from patients suffering from influenzal meningitis are shown in Table II.

In these tests, a series of four tubes was set up. Five drops of doubling dilutions of *Hæmophilus influenzæ* (type *b*) rabbit antiserum were placed in each row. In the control row, five drops of normal saline solution were added to each tube; in each of the remaining rows, five drops of the specimen of cerebro-spinal fluid under test. One drop of sensitized fowl erythrocytes was then added to all the tubes. The dilutions of antiserum were so chosen that the erythrocytes in the final tubes of the control row showed only partial agglutination, indicating that a limiting dilution of antiserum was present in this tube. It will be noted that in every instance the presence of cerebro-spinal fluid from patients with active influenzal meningitis effected a reduction in the agglutination titre of the antiserum for the sensitized cells. Twenty-five

TABLE I.
The Inhibitory Effect of Polysaccharide on Hæmagglutination.

Polysaccharide Dilutions. (Five Drops.)	Dilutions of Serum (Five Drops).[1]								
	1/25	1/50	1/100	1/200	1/400	1/800	1/1600	1/3200	1/6400
10^{-5}	+++	+++	±	−	−	−	−	−	−
10^{-6}	+++	+++	+++	+++	++	−	−	−	−
10^{-7}	+++	+++	+++	+++	+++	+++	±	−	−
10^{-8}	+++	+++	+++	+++	+++	+++	+++	+	−
Control saline solution (five drops)	+++	+++	+++	+++	+++	+++	+++	+	−

[1] After mixing, one drop of sensitized fowl erythrocytes was added, the tubes were shaken, and results were read at 60 minutes.

TABLE III.

Influenzal Meningitis: Response to Treatment as Indicated by the Hæmagglutination Test.

Subject.	Days in Hospital.													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
D.S.	2[1]	2	2	1	0	—	0	—	0	0	0	—	—	—
W.B.	3	3	2	1	—	—	0	0	0	0	—	0	—	0
E.S.	2	1	1	0	—	—	—	0	—	—	0	1	—	0
J.D.	3	2	—	—	—	—	0	0	0	—	—	—	—	—
K.W.	3	2	1	—	—	—	—	—	—	—	—	—	—	0
P.B.	2	1·5	—	—	—	—	—	1	—	—	—	—	—	—
N.G.	3	1·5	—	—	0	0	0	0	—	—	—	—	—	—
G.C.	3	2	—	1	—	0·5	0·5	0	—	—	0	—	—	0

[1] Figures refer to the number of tubes in which the inhibition occurred.

specimens from patients with non-influenzal meningeal infections gave completely negative results, as did numerous specimens of cerebro-spinal fluid obtained from patients on whom lumbar puncture had been performed for reasons other than suspected meningeal infection. It is our custom in recording results to grade positive specimens as "1+", "2+" or "3+" according to the number of tubes in which inhibition of agglutination is evident; such figures are shown in the last column of Table II.

Examinations of successive specimens of cerebro-spinal fluid from patients under treatment for influenzal meningitis show that as the patients respond to treatment the concentration of bacterial polysaccharide falls. The results of such examinations are shown in Table III. Except in an occasional case in which a relapse occurred, once the result had become negative it remained so until the patient's discharge from hospital.

TABLE II.

Results Obtained with the Hæmagglutination Test on Initial Specimens of Cerebro-spinal Fluid from Subjects with Influenzal Meningitis.

Specimen.	Dilutions of Serum.				Result of Test. (Number of Tubes in which Hæmagglutination is Inhibited.)
	1/200	1/400	1/800	1/1600	
D.S.	+++	+	–	–	2+
W.B.	–	–	–	–	3+
G.J.	+++	++	–	–	2+
E.M.	+	–	–	–	3+
E.S.	++	–	–	–	2+
J.D.	–	–	–	–	3+
K.W.	–	–	–	–	3+
P.B.	+++	++	–	–	2+
P.F.	–	–	–	–	3+
N.G.	–	–	–	–	3+
N.B.	++	–	–	–	3+
K.M.	+++	++	–	–	2+
G.C.	+++	+	–	–	2+
K.D.	–	–	–	–	3+
D.G.	+++	+++	+	–	1+
Saline solution control	+++	+++	+++	+	

Methods.

Undegraded polysaccharide of *Hæmophilus influenzæ* (type *b*) is prepared as follows.

Ten millilitres of Levinthal broth are inoculated in a 250 millilitre Erlenmeyer flask with a loopful of a fully mucoid strain of *Hæmophilus influenzæ* (type *b*), the whole being incubated overnight at 36° to 37° C. From this culture Levinthal agar plates are heavily seeded and incubated at 37° C. for six or seven hours, by which time a confluent fluorescent growth should be present. The organisms are scraped off and suspended in 90% phenol solution, one millilitre of phenol solution being used to the growth from each plate. The phenol suspension is placed in a boiling water bath for ten minutes, cooled and centrifuged. The supernatant fluid is discarded. The deposit is washed once with 90% phenol solution, once with ethyl alcohol and twice with ether to remove the phenol and dry the precipitate, and extracted with a quantity of water equal in volume to the phenol solution used for purification, the insoluble material being removed by centrifugation or filtration with the aid of super-cel. Reprecipitation is effected with three volumes of alcohol after a few drops of a saturated aqueous solution of sodium acetate have been added. The polysaccharide so obtained is washed with alcohol and ether and kept under seal or in a desiccator.

Erythrocytes are sensitized with the polysaccharide in the following manner.

A 1:1000 dilution of polysaccharide in neutral 0·5% formol saline solution is prepared. Twofold dilutions of the polysaccharide ranging from 1:2000 to 1:256,000 in small glass tubes are prepared, nine drops to each tube. To each tube one drop of packed washed erythrocytes is added—fowl erythrocytes for preference, since they form a sediment rapidly, but human erythrocytes are suitable. The mixture is then allowed to stand for five to ten minutes. All tubes are centrifuged, the erythrocytes are washed twice in normal saline solution, and the deposited erythrocytes are resuspended in each tube in 19 drops of normal saline solution to obtain a 5% suspension.

In a corresponding number of fresh tubes are placed ten drops of a 1:200 dilution in saline solution of a high titre rabbit influenzal antiserum. To each tube is added one drop of the suspensions of erythrocytes which have been sensitized with varying dilutions of polysaccharide. The contents are well mixed and the tubes are allowed to stand on the bench until sedimentation of the erythrocytes is complete (from thirty to sixty minutes if fowl erythrocytes are used, from one to two hours if human erythrocytes are used). The tube containing the highest dilution of polysaccharide in which the erythrocytes are completely agglutinated is noted. This will normally be in the neighbourhood of 1:64,000 dilution of polysaccharide.

For the test proper, one volume of packed washed erythrocytes is treated with nine volumes of a polysaccharide solution eight times as concentrated as that just capable of sensitization. If the concentration of polysaccharide in the last tube in which complete agglutination occurred was 1:64,000, a 1:8000 dilution of polysaccharide would be prepared for sensitization of the cells for the main test.

Antiserum is titrated as follows.

A 5% suspension of erythrocytes sensitized with the dilution of polysaccharide just determined is prepared. Graded dilutions of *Hæmophilus influenzæ* (type *b*) rabbit antiserum are prepared from 1:200 to 1:6400 or higher if necessary. To ten drops of each antiserum dilution, one drop of 5% sensitized erythrocytes is added. The two are mixed and allowed to stand, and the final agglutinating titre of the antiserum to the sensitized erythrocytes is read.

The test proper is performed in the following way.

A 5% suspension of erythrocytes sensitized as previously determined is prepared. A dilution of antiserum sixteen times as concentrated as its previously determined titre is prepared (for example, if the agglutinating titre was 1:3200, a dilution of 1:200 is prepared). In each initial tube of as many sets of four tubes as there are specimens for test, *plus* a control set, five drops of this dilution are placed, and five drops of doubling dilutions in the succeeding tubes. To each of the four tubes in the control row, five drops of saline solution are added. To each tube in the test rows five drops of the cerebro-spinal fluid under test are added. To all tubes is added one drop of the 5% suspension of sensitized erythrocytes. The tubes are shaken and allowed to stand on the bench until the cells have settled. The end agglutination titre of the serum to each row of test and control tubes is read. Rows containing cerebro-spinal fluid in which there is no inhibition of the antiserum are read as "negative", rows

in which the titre of the antiserum is less than in the control are "positive". If control rows are included in which polysaccharide in known dilutions has been added—say 1:1,000,000 and 1:10,000,000, an approximate estimation of the polysaccharide content of the specimens can be made.

If there is doubt in any specimen as to whether or not there is a trace of inhibition, the test on that specimen may be repeated with half the dose of sensitized erythrocytes—that is, one drop of a 2·5% suspension of sensitized erythrocytes being added instead of one drop of a 5% suspension. There will rarely be any doubt in the first specimen tested from a patient with acute influenzal meningitis, but with later specimens from patients under treatment, it may be necessary to adjust the conditions to maximum sensitivity if it is desired to detect traces of polysaccharide.

Discussion.

This test is based on the detection of the polysaccharide of *Hæmophilus influenzæ* (type *b*) in specimens of cerebro-spinal fluid. It does not differ in principle from the method of diagnosis in which the precipitin reaction between the polysaccharide in the cerebro-spinal fluid and the specific antiserum is utilized. It has advantages over the precipitin reaction, since it is considerably more sensitive. In our experience, polysaccharide in a dilution in normal saline solution of between 1 in 1,000,000 and 1 in 5,000,000 shows a just detectable ring with a good serum, when the test is performed under the best conditions, and is not complicated by the turbidity or coloration which may be present in specimens of cerebro-spinal fluid. The test described permits the detection of polysaccharide in a dilution of 1 in 10,000,000 or more, and the end point of the reaction is unmistakable. We have not encountered a single false positive reaction in some hundreds of specimens examined. We did, in the early stages of development of the test, before it had become adjusted to the proper sensitivity, obtain an occasional false negative reaction; with the method described in this report, all specimens from patients with untreated influenzal meningitis have given positive results.

The directions for preparation and standardization of the reagents as set out above may appear somewhat formidable for a procedure which in many hospitals may be required only on rare occasions. The polysaccharide solution in formol-saline solution and antiserum are both stable reagents provided that they are kept sterile and in the cold, so that only an initial standardization is necessary. The test has, in fact, been employed as a routine in the clinical laboratory of the Children's Hospital, Melbourne, for some months.

This test has the advantage that the diagnosis of influenzal meningitis may be confirmed or excluded with certainty within an hour of receipt of a specimen of cerebro-spinal fluid in the laboratory. Diagnosis at the earliest moment, with immediate institution of specific therapy, is essential if the best results are to be obtained in treatment of this infection.

The test as described is not applicable to the diagnosis of the rare meningeal infections with *Hæmophilus influenzæ* of types other than *b*. It can be adapted to this end by use of the specific polysaccharides of these types, but they are so rarely seen that it is more practical to rely on cultural investigation of the cerebro-spinal fluid in such infections.

Summary.

1. A test is described for diagnosis of influenzal meningitis which is based on the fact that the capsular polysaccharide of *Hæmophilus influenzæ* (type *b*) is present in the cerebro-spinal fluid in sufficient concentration to inhibit agglutination by specific antiserum of erythrocytes previously sensitized with the polysaccharide.

2. The results of the application of this test in the laboratory diagnosis of influenzal meningitis are described.

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CONGENITAL STEATORRHŒA DUE TO DEFECT OF THE PANCREAS.[1]

By MARGARET HARPER,
Sydney.

FOR this paper I have chosen the title which indicates the presenting symptom and its connexion with the pancreas; other names appear to mislead many. The term "cœliac syndrome", used widely since Dorothy Andersen's report in 1938, has led to a great deal of confusion. Some Americans have tried to point out the mistake of using this term in connexion with congenital pancreatic steatorrhœa. Parmalee in 1935 reported two cases confirmed at autopsy and remarked that "a study of the literature plainly shows the confusion regarding the clinical conditions classified as cœliac disease". He adds that it is with the hope of aiding in establishing a correlation between the clinical and the pathological picture that his two cases are reported. He concludes that this disease has a symptomatology and a clinical course quite different from those of cœliac disease. Kramer and Farber also have pointed out that there is sufficient evidence for a complete separation of idiopathic cœliac disease from congenital pancreatic steatorrhœa.

It is only in recent years that the clinical symptoms of congenital steatorrhœa have been connected with the pancreatic defect. The first two Sydney cases were reported in 1930 with the post-mortem examination in one of them, which revealed the so-called cystic fibrosis of the pancreas. In 1938 eight more Sydney cases were reported with post-mortem examinations in five. Later in the same year Andersen's article from the pathological laboratory of the Babies' Hospital, New York, reported 49 cases culled from various sources; it is written from the pathological standpoint without personal clinical experience of the disease.

In Sydney our approach was clinical, with the support of the department of pathology of the Royal Alexandra Hospital for Children. Hence we were able to avoid the confusion induced by the use of the term "cœliac syndrome".

I hope to be able to show in this paper, based on 42 cases, that this disease can be diagnosed clinically from the neo-natal period.

Of the 42 cases of which records are available, Table I shows the ages at which these babies were first seen. These cases were diagnosed clinically and in all which came to autopsy the diagnosis was confirmed. Of the eight patients seen in the neo-natal period, five have died and the diagnosis was confirmed at autopsy.

The oldest child was first seen at thirteen months and therefore was at an age when cœliac disease might occur, but clinically there was no suggestion of this condition.

Her birth weight was six pounds three and a half ounces and her weight at thirteen months was fourteen pounds. She had not received any treatment for her failure of nutrition except a large number of changes in her diet. She had frequent motions, as many as five bulky stools a day. Her height and her head circumference were normal for her age, but the circumferences of her chest and of her abdomen were both three inches below the normal. It is thus evident that there was no abdominal distension. The report of the examination of her stool was as follows: "Canary yellow oily bulky stool with numerous undigested

[1] Read at a meeting of the Section of Pædiatrics and the Section of Pathology, Bacteriology, Biochemistry and Experimental Medicine, Australasian Medical Congress (British Medical Association), Sixth Session, Perth, August, 1948.

food particles visible macroscopically." On microscopic examination large numbers of fat globules were seen. The total fat content was 46% of dried fæces. Unsplit fat was 60% of total fat. This patient is now eight years old, but she was seen recently in the out-patient department of the Royal Alexandra Hospital for Children with a chronic respiratory infection with indications of the presence of bronchiectasis.

In the neo-natal period, the babies appear normal. Their birth weights are usually within normal limits. The main complaint is that the baby has lost a considerable amount of weight in spite of taking adequate amounts of breast milk with an eager appetite. Normal bowel actions may be reported even by experienced nurses, and unless the medical adviser inspects the stools himself, having already made himself familiar with the appearance of the normal newly-born infant's stools, the diagnosis may not be suggested. We have had three babies with congenital steatorrhœa, two from the same family, from one maternity hospital, because the sister in charge of the babies had recognized the abnormality of the stools and the unusual loss of weight of the babies.

TABLE I.
42 Cases: Age at which Patient First Seen and Condition Diagnosed.

Age in Months.	Number.
Under 1 (neo-natal)	8
1 to 3	9
3 to 6	14
6 to 9	6
9 to 12	4
13	1
Total	42

Male, 22; female, 20; post-mortem examination, 18 cases.

The motions are frequent. Stools may be passed five or six times daily. They are large and bulky—homogeneous and pale cream or pale yellowish green. They may be pale yellow when passed, becoming pale green on exposure to air. They have a glistening, greasy appearance and oil may be present.

The total amount of fæces passed in the twenty-four hours is greatly in excess of the normal, and it is evident that the baby is losing a great deal of the food he takes so eagerly.

The odour of the stool is rancid at this stage.

The history of one of these babies first seen when ten days old is that she appeared normal at birth, weighing seven pounds six ounces. At three weeks of age she weighed six pounds eight ounces, in spite of taking well over her theoretical caloric requirement of her mother's milk.

The stools were large, consisting of a homogeneous greasy mass of a peculiar dark yellowish green colour. Three to six of these stools were passed daily.

The report on the biochemical examination of the stool made when the baby was twenty-four days old was as follows: "Soft greasy stool of greenish yellow colour. Odour, rancid. Microscopically numerous fat globules were seen and some fatty acid crystals. Total fat of dried fæces was 63·7%. Unsplit fat was 50·1% of the total fat."

After the neo-natal period, if the baby continues to be breast fed, the stools may become more normal in appearance and mothers are inclined to describe them as normal, although their size may still be large and they may be frequently passed.

I have seen normal yellow stools passed by some of these babies which would not suggest steatorrhœa. It is known that breast milk contains active enzymes, lipase, amylase and others. Holt considers that their importance is questionable. Murlin, however, writes:

> It should be borne in mind that human milk itself contains an active lipase, and with the stomach lipase, a very lively lipolysis may take place in breast-feeding, so that one-quarter or more of the entire fat of the milk may be split up before the food leaves the stomach.

Whatever the reason, the fact remains that the stools of the breast-fed infant may, for a period, appear normal in colour and consistency even if there is pancreatic achylia. The size and frequency of the motions may be still increased and the baby's gains in weight not satisfactory.

In none of the neo-natal cases in this series has there been any evidence of meconium ileus.

Farber makes the statement in several articles that if pancreatic achylia is present before birth, a physically altered meconium will result which will cause intestinal obstruction shortly after birth. If the achylia is not present until after the neo-natal period, the disease picture will be that of congenital pancreatic steatorrhœa. This hypothesis ignores the neo-natal onset of the symptoms.

In confirmation of the connexion of meconim ileus with pancreatic achylia, Dr. Reye, director of the department of pathology at the Royal Alexandra Hospital for Children, and others have found the typical lesions of the pancreas in cases of meconium ileus, but these cases are rare.

The usual history of the baby seen at later ages is that "he has never done well". His weight has not increased at a satisfactory rate, although his appetite is good. Numerous different foods have been tried without success. The mother may say that he has "diarrhœa". Sometimes the breast-fed baby will do fairly well until the usual weaning time, although his gains in weight may be small and irregular and he has not reached his expected weight for age and birth weight. In such cases the mother may say that the stools are normal, especially if the baby is her first. On investigation of the fæces and their size and frequency of passage the diagnosis is suggested.

The stools are similar to those passed in the neo-natal period with the expected alterations depending on the type of food the baby is having. They have the same greasy, pale, yellowish-green appearance and oil may be passed with the stool or separately. They are bulky and large. The odour varies from the rancid to the penetrating putrefactive.

The mother occasionally volunteers the statement that oil is passed. She also may say that the napkins are difficult to wash.

The significance of the excretion of oil and of the numerous fat globules seen microscopically is still an undecided question. Some authorities regard the oil and fat globules as neutral fat, but this is not generally accepted. Thaysen says that the oil passed in pancreatic fatty diarrhœa is largely composed of neutral fat. Vaughan Harley found it to consist for the most part of fatty acids with only small quantities of neutral fat and soaps. It is, however, generally accepted that the passage of "butter stools" is intimately associated with lesions of the pancreas, although Thaysen concludes that it constitutes a symptom of excessive fat evacuation rather than a symptom of pancreatic disease. It is not found either in cœliac disease or in sprue. Of the 42 cases in this series the excretion of liquid fat was noted in 25.

Vomiting is not a presenting symptom, although it does occur sometimes and may be rather persistent. If present, it usually ceases when the baby is having a suitable diet.

The appetite is good and fails only when the child develops a respiratory infection or some other illness.

Loss of weight is usually marked, or rather failure to gain satisfactorily, and is usually the cause of the mother's seeking medical advice. The emaciation of some of these babies may be extreme, but in others it may be surprisingly slight. It is more common to find a small, irregular gain with the child considerably under its expected weight.

Abdominal distension is not particularly marked during the first year. It seems to become greater after the first year if the child has been untreated. I have not seen it present in anything like the same degree as is usual in cœliac disease. The babies often appear happy and contented and the plumpness of the face is often deceptive.

The respiratory symptoms which so far have always ended the scene may be reported as being present with

an unproductive cough from birth. More commonly this symptom appears later, and if dietetic treatment is begun early and the child's nutrition is kept in a satisfactory state, it may be delayed for some years.

The outlook is poor for infants who when first seen have a respiratory infection. The cough begins as an unproductive spasmodic cough which resembles whooping cough, and is sometimes mistaken for this. At this stage there is little to be found on examination of the lungs. The process is revealed more by coarse sticky râles and asthmatic type of breath sounds due to obstruction of the bronchioles with exudate. Emphysema develops and areas of atelectasis may be seen radiographically. Where the diagnosis of congenital pancreatic steatorrhœa has not been made before the child's admission to hospital it is natural perhaps that the condition of the lungs takes all the attention and when death occurs the diagnosis of bronchopneumonia is made. The pancreas at autopsy may not be examined because to the naked eye it may appear normal.

Diagnosis.

An adequate history of the child's progress from birth should be taken. A history of the stools should be gone into carefully. This will often supply indications of the correct diagnosis.

The one condition indispensable in making the diagnosis of congenital pancreatic steatorrhœa is a personal examination of the stools interpreted in the light of the clinical examination of the child. The size, colour, consistency, odour and frequency should all be noted. Diarrhœal stools are seen only when the child has a digestive upset or an infection.

Biochemical Examinations.

The stool is examined for fat. It does not appear necessary to have a twenty-four-hour or three-day specimen examined. If taken into consideration with the clinical examination of the child, examination of one specimen usually gives sufficient information. It may be helpful to have another stool examined at a later date. Table II, from 35 records of biochemical examination of stools for fat from infants and children with congenital pancreatic steatorrhœa, gives an idea of the variations which may occur in such examinations.

TABLE II.

Observation.	Number of Patients.
Total fat of dried fæces (percentage):	
60 to 80	12
40 to 60	19
20 to 40	4
Total	35
Percentage of total fat unsplit:	
60 to 82	11
30 to 60	17
30 or less	7
Total	35

In 28 of these 35 cases the unsplit fat content was above normal. Microscopic examination showed the fat globules to be numerous to very numerous. Fatty acid crystals were few in number. Soap plaques were rare. "Butter stools" (oil) were noticed in 25 cases.

In a case in which the total amount of fæces excreted in twenty-four hours was examined the weight of dried fæces was 96 grammes, the weight of total fat was 23·4 grammes, the weight of neutral fat was 15 grammes. In no case was a percentage of unsplit fat within normal limits taken as evidence for an alteration of the clinical diagnosis.

Other Biochemical Investigations.

Examination of duodenal contents for pancreatic enzymes may be undertaken. If little or no trypsin is found in the duodenal contents, defective excretion of pancreatic juice is suggested. This absence or reduction below the normal amount of trypsin in the duodenal juice has been found in all cases of so-called cystic fibrosis of the pancreas investigated in this way. The results in cœliac disease are normal. In none of this series of cases was this investigation carried out. The procedure is long and exhausting, and it would not have been of material help in any of these cases.

There may be rare cases in which this investigation may be helpful, even if not necessary, but in my experience so far it has not been so.

Examination of the fæces for protein-splitting ferments does not appear to be reliable. "In a certain number of healthy individuals no such enzymes can be detected and in the rest a wide range of variation is obtained. It would appear, therefore, that results characteristic of pancreatic lesions do not exist" (Harrison, 1947). The fæces must be examined as soon as they are passed—not more than an hour after evacuation—since the enzyme activity rapidly deteriorates.

Estimation of the amount of diastase in the urine is of value only in acute conditions. The diastase content is normal or low in chronic conditions.

My experience leads me to believe that if it is recognized that congenital pancreatic steatorrhœa is a definite entity, the symptoms of which occur from birth, the diagnosis can be made clinically, often before the onset of the respiratory infection (see Table III).

TABLE III.

	Congenital Pancreatic Steatorrhœa.	Cœliac Disease.
Age of onset ..	From birth.	From nine months.
Appetite	Usually good.	Poor.
Pulmonary infection	Frequent.	Not abnormally frequent.
Pancreatic enzymes ..	Absent or diminished.	Normal.
Gheese tolerance test..	Result, normal or "flat" curve.	"Flat" curve.
Fæcal fat	High percentage, often poorly split.	High percentage, well split.
"Butter stool" (oil) ..	Frequent.	Not present.
Usual outcome ..	Death from respiratory infection.	Recovery.
Familial incidence ..	Frequent.	Rare.
Autopsy	Lesion of the pancreas.	No lesion of pancreas.

The Family History.

It has long been recognized that this condition is a familial one. Garrod in 1912 drew attention to this. The usual inquiry into the family history should be carefully carried out, with special attention to siblings who have died in infancy. Table IV shows the family history in 13 cases of this series. There are other conditions in infancy and young childhood in which steatorrhœa occurs, such as congenital obliteration of the bile ducts, prematurity, when excess of fat is given in the food, and a temporary inability to digest a normal amount of fat, usually the result of unsatisfactory feeding or of gastro-intestinal infections as well as cœliac disease. These should all be kept in mind and confirmed or excluded by clinical examination.

Pathology.

The pancreas may appear normal to the naked eye. It may be thinner, firmer and more granular than normal. Rarely small transparent cysts of pinhead size may be seen. In only two of this series were these noted.

Microscopically the acini and ducts show all degrees of dilatation and distortion. The lumina are filled with structureless material which suggests inspissated secretion. Interlobular and interacinar connective tissue is increased. Islet tissue is normal. There has been no evidence in this series of cases of obstruction of the main ducts, such as

TABLE IV.
Family History.

Patients.	Pregnancy.	Siblings Affected.	Healthy.	Mother's Report.
1. Brother	Second	—	—	First child died of neo-natal infection.
Sister	Third	—	—	
2. Brother	First	—	Third and fourth	
Sister	Second			
3. Two brothers	Third	2 elder probable.	Fourth	First two children died of same symptoms.
One sister	Fifth	—	—	
	Sixth	—	—	
4. Brother	First	—	Third	
Sister	Second	—	—	
5. Two boys	First	—	Third	
	Second	—	—	
6. Boy	Sixth	3 probable.	2	Three died of "bronchial trouble". "Same stools."
7. Girl	Seventh	2 probable.	4	Third and sixth died of wasting. "Could not digest fat."
8. Girl	Fifth	2 probable.	2	Both similar stools. "Pertussis" and pneumonia.
9. Boy	Third	1 probable.	2	Second "never did well". "Pertussis" and pneumonia. No history of contact with pertussis.
10. Girl	Fourth	1 probable.	2	Second baby "never did well". Died of pneumonia.
Possible.[1]				
11. Girl	Second	1 possible.	None	First died of congenital intestinal obstruction.
12. Girl	Third	1 possible.	1	Second died of congenital intestinal obstruction.
13. Boy	First	1 possible.	1	Third died of congenital intestinal obstruction.

[1] It is possible that these three died of meconium ileus associated with "cystic fibrosis of the pancreas".

occurs in congenital atresia, or malformation of the ducts, such as may occur in the annular pancreas. It appears that the secretion of the acini is abnormal and becomes inspissated in the small ducts and the acini, thus obstructing the outflow of the pancreatic enzymes.

Andersen's colleague Beryl Paige has examined the pancreas in 346 consecutive autopsies on fœtuses and still-born babies, but has not found any evidence in these of the so-called cystic fibrosis of the pancreas.

The condition of the lungs at autopsy has features which suggest that the pancreas should be examined. During the last seven years Reye has examined the pancreas in all cases in which the lungs appear bilaterally emphysematous. This emphysema may be so marked that the lungs are distended to fill the thorax and pressure marks of the ribs are evident on the surface. The lungs may entirely cover the ventral surface of the heart. In a recent examination the inferior edge of the liver was three inches below the costal margin. This organ had been pushed downward and tilted to the right because of the pulmonary emphysema. There was no hepatic enlargement.

In practically all cases the liver shows fatty changes which, if the child survives to a later age, may pass on to cirrhosis.

Reye has examined the salivary glands in a number of cases, but has so far found no evidence of the changes described by Farber. Neither he nor Andersen has been able to confirm Farber's suggestion that the secretions of the bronchial mucosa are defective in a manner similar to the pancreatic secretion.

Andersen says that the bronchial glands appear normal in most cases.

Reye is of the opinion that the infection of the lungs, always present, obscures the picture so that it is impossible to make a statement on the condition of the bronchial glands; whereas the examination of the lungs in two cases of death due to meconium ileus with cystic fibrosis of the pancreas but with no respiratory infection revealed nothing abnormal in the bronchial glands.

During the five-year period January, 1943, to December, 1947, the number of autopsies performed at the Royal Alexandra Hospital for Children was 755. Twenty-three cases of congenital pancreatic steatorrhœa were found (3·04%). Andersen reports the same percentage in several hospitals in the United States of America.

The age at death was from five days to three years. The number of patients under twelve months of age was 18 the number between twelve and twenty-four months was four, and between twenty-four and thirty-six months, one. Cases diagnosed clinically numbered 11; cases diagnosed only at autopsy numbered 12. The case in which death occurred at the age of five days was one of meconium ileus.

Pathogenesis.

The pathogenesis of this condition remains obscure and we await further elucidation.

Congenital stenosis or atresia of the main pancreatic ducts or malformations of the duct system associated with an annular type of pancreas are rare causes of pancreatic achylia.

Farber's suggestion that congenital steatorrhœa caused by the so-called cystic fibrosis of the pancreas is a systemic disease affecting the lungs, liver and other organs is an interesting hypothesis. He thinks that a disturbance of the parasympathetic innervation, or perhaps more accurately an autonomic imbalance in the nervous control of secretion in the pancreas and in mucous glands, may be the cause. He and his collaborators are continuing their investigations.

That there must be a connexion between the condition of the pancreas and the condition found in the lungs which brings about the deaths of these patients seems evident.

The lack of absorption of vitamin *A*, at first suggested as the cause of the respiratory infection, does not account for it, as the presence of squamous metaplasia of the epithelium of various organs has been found in few of the patients.

Treatment.

There are two obstacles to the successful treatment of these cases in the present state of our knowledge. The lesion in the pancreas persists throughout the life of the patient. No improvement has been noted to occur, by direct estimation of the enzymes, even after the nutritional state has been restored to normal. Secondly, the pulmonary lesion, once it becomes firmly established, is of a type which responds poorly to treatment, so that it is likely to progress and cause death. After the respiratory infection is established, the state of nutrition fails and cannot be again brought to normal. These children do not die of malnutrition, but from the effects of the chronic respiratory infection.

The treatment is dietetic. These children require more food than the normal amount. When the pancreatic enzymes are lacking, the amount of food absorbed increases to some extent with increased intake and with the control of the number and size of the stools. The appetite is often ravenous and should be satisfied.

If a baby is artificially fed when first seen and the condition is diagnosed, the use of separated milk made with "Benger's food" gives satisfactory results. Young infants in this way can take a mixture with high protein content balanced with carbohydrate and can gradually get on to the full-strength separated milk with "Benger's food". Additional carbohydrate may be added in the form of sugars such as dextrimaltose, lactose or glucose.

With regard to the fat in the diet, it should be kept at the level at which the size and number of the stools approach the normal. If given in excess of this amount, it is rapidly excreted, carrying with it a considerable amount of food which would otherwise be digested and absorbed. The intestinal juice contains small but not unimportant amounts of lipase, and some fat in the diet can thus be utilized even when pancreatic achylia is present.

Egg yolk is given early, added to the milk mixture. Later it may be possible to replace some of the separated milk by whole milk. The child should have the ordinary diet for his age with restriction of fat. As much fat should be given as possible, but this is always a limited amount and may have to be varied from time to time.

The use of enzyme preparations, such as pancreatin, is of uncertain value because of the variability of the potency of the preparations, and the fact that the enzymes are inactivated by the acid in the stomach.

In the cases under review in this paper there was little difference in the state of nutrition of the babies who were given and those who were not given pancreatin in limited dosage. It may be that the pancreatin will digest some of the food that would otherwise be lost and thus be of some help.

Several investigators maintain that vitamin *A* is absorbed better when it is administered in a non-fatty menstruum. Preparations of this sort are now available and it seems worth while to use them in these cases. Exposure to sunlight should be carefully carried out to maintain the supply of vitamin *D*.

Treatment of the pulmonary infection has been unsuccessful. With the use of the sulphonamide drugs and penicillin these children can be carried over several periods of exacerbation of the respiratory infection, but recurrences take place and later, sometimes after some years of invalidism, they succumb to the pulmonary lesions. This type of pulmonary infection appears to be incurable.

Of this series of 42 patients eight are known to be alive. The ages range from one to nine years and only two of them are free from chronic respiratory infections. These two are five and one and a quarter years old.

Reviews.

CORRELATIVE NEUROANATOMY.

"CORRELATIVE NEUROANATOMY", by J. J. McDonald, J. G. Chusid and J. Lange, is described, according to the publishers, as "A comprehensive manual for the student in gross anatomy, neuroanatomy, neurodiagnosis and neurology which correlates the anatomical and physiological background with the clinical findings of neurological disorders".[1] The orderly classification which is implicit in such an attempt to present neuroanatomy, neurodiagnosis and neurology comprehensively in 150 pages will evoke a sense of revulsion in some minds and welcome in others. The reactions which it will evoke illustrate the variability of the human mind. The student who is able to absorb quickly and retain such classifications as are presented here, often produces envious despair in the student of slower pace. Yet the latter has qualities which enable him to compete in examinations successfully, and perhaps to be evaluated even more highly in his post-graduate life. Some can benefit from what is presented here—others are incapable of profiting by it.

The trend of medical education, and indeed of education in general, is to avoid burdening the student mind with too much detail, but rather to teach principles which will allow him the better to profit from experience. There is a limit to the receptiveness of most minds, a fact which is often forgotten by the specialist in preparing a book for the use of the student. It may be recalled that Sherlock Holmes astonished the faithful Watson by denying knowledge of the Copernican theory and of the composition of the solar system. He explained that, like an attic, his brain had a certain capacity, and he refused to burden it with matters which would be useless to him, lest more important things be excluded. Sherlock Holmes went on to explain that "the skilled workman is very careful indeed as to what he takes into his brain-attic. He will have nothing but the tools which may help him in his work, but of these he has a large assortment and all in the most perfect order". Thus, the information imparted would be of value if it could be stored and used properly. More than most books, the value of "Correlative Neuroanatomy" to the individual will depend upon the individual's psychology.

The condensation of the existing mass of neurological data into 150 pages, diagrams included, is evidence that scarcely a word is wasted. The condensation has been efficient. The first section deals with the cranial and peripheral nerves and contains a number of excellent diagrams. The second section deals with anatomical and physiological factors in localization and deals extensively with syndromes and reflexes, many of which the neurologist rarely sees or uses, although he may employ some of the latter to beguile his student's clinic. We are told that intracranial pneumography (amongst a number of other subjects) is thoroughly outlined. These two pages would have been better omitted. The section on electroencephalography is longer, and almost two of its four pages deal with systems of analysis of the tracings. The third section has been completely rewritten and enlarged; it deals with diseases of the nervous system and covers 27 pages. It will hardly assist the student to a better understanding of the patient who comes asking for help.

On the whole, the information given is as accurate as our present state of knowledge and the brief presentation allow. Errors are few. However, by a curious chance it failed to help a student to make an accurate diagnosis in the first case presented in a neurological clinic to which the book was introduced for trial. The patient had tubular visual fields with little retinal pigmentation, which had not been seen with the ophthalmoscope. *Retinitis pigmentosa* is not mentioned as one of the causes of "circumferential blindness", this finding being ascribed to hysteria or retrobulbar neuritis. The brevity of the chapter on neurology may be still more confusing to the student who is not in the position to benefit from shorthand, since he has not yet learned the vocabulary and phrasing of clinical neurology.

However, in spite of all this, there is a function which the book usefully performs. It will be found to serve as a small, flexible book of reference for all those who cannot carry in their minds the anatomical details which are concisely summarized and admirably illustrated within its covers. This, after all, is what is to be expected from the title "Correlative Neuroanatomy".

[1] "Correlative Neuroanatomy", by Joseph J. McDonald, M.S., M.Sc.D., M.D., Joseph G. Chusid, A.B., M.D., and Jack Lange, M.S., M.D.; Fourth Edition; 1948. California: University Medical Publishers. 7" x 9", pp. 160, with illustrations. Price: $3.00.

CHEST EXAMINATION.

IN recent years there has been an increasing tendency for physicians interested in chest diseases to rely more and more on X-ray films with increasing neglect of fundamental clinical signs. "Chest Examination", by R. R. Trail, the third edition of which has just been published, is a salutary reminder to all that the eyes and ears still have a valuable place in the examination of the patient himself who is suspected of pulmonary disease.[1]

The book is divided into four sections: (i) applied anatomy, (ii) physical examination, (iii) the abnormal film, and (iv) applied pathology. In each section the author has endeavoured to correlate findings, whether clinical or radiological, on the underlying pathological process. As an example, he has constantly reiterated the significance of the sterno-mastoid sign and the mechanical principles causing the sign, based on anatomical studies of the pretracheal fascia and its continuity with the deep fascia of the neck and the peribronchial elastic tissues.

In the section on physical examination it is pleasing to note the author's insistence on the value of all methods of examination. Many physicians will support this observation, particularly the importance of a thorough inspection of the patient, special attention being paid to the development of the chest, its movement on respiration, the presence or absence of the sterno-mastoid sign, and the presence or absence of clubbing of the fingers.

[1] "Chest Examinations: The Correlation of Physical and X-Ray Findings in Diseases of the Lung", by Richard R. Trail, M.C., M.A., M.D. (Aberd.), F.R.C.P. (Lond.), with a foreword by Sir Walter L. Langdon-Brown, M.A., M.D., F.R.C.P., D.Sc., LL.D.; Third Edition; 1948. London: J. and A. Churchill, Limited. 8½" x 5½", pp. 184, with illustrations. Price: 12s. 6d.

The author makes the statement that many students concentrate too much on the stethoscope. He then proceeds, in Chapter VII, to a rather lengthy description of the types of abnormal sounds heard, and elaborates a scheme by which he has endeavoured to interpret in pathological terms the underlying morbid process. This chapter is perhaps the most controversial; but the author at least makes a constructive attempt to interpret auscultatory abnormalities.

The section on applied pathology is excellent, and in a brief description of all the common chest diseases, the underlying pathogenesis is stressed.

The book is well illustrated with 115 diagrams and reproductions of skiagrams of the chest. It is of 170 pages; the subject matter throughout gives constant food for thought. It is therefore highly recommended to all physicians interested in chest diseases. In his preface, the author states his desire to help the student undergraduate and post-graduate. It is thought that the publication will be of greater benefit to the more advanced student in medicine.

BLOOD DERIVATIVES AND SUBSTITUTES.

"BLOOD DERIVATIVES AND SUBSTITUTES", by C. S. White and J. J. Weinstein, with acknowledged contributions in certain sections from other leading American authorities, is a volume in which more ground is covered that the title suggests.[1] The authors introduce their subject by tracing briefly, with emphasis on the part played in the United States of America, the history of transfusion of blood, and the developments so dramatically accelerated and intensified during the recent war, which have given blood and plasma and the fractions of the latter the status they occupy in present-day therapeutics.

Basic principles concerned in the chemistry and physiology of whole blood and plasma and its derivatives or substitutes, and their role in the treatment of shock and other pathological conditions, are given well-balanced consideration.

There are chapters on the administrative aspects of the collection, storage and transportation of blood, and on the care of blood donors.

A wide range of technical procedures is described in great detail with a clarity and vividness which are most impressive. Perusal of this book leaves the reader with a feeling closely akin to the satisfaction derived from a visit to a laboratory, in which he has been given the opportunity of seeing in actual operation all the technical methods used, some of which are original and ingenious, and of discussion with hospitable officers willing to share freely their personal knowledge and experience. Those in charge of the organization and operation of blood and plasma (or serum) "banks" will therefore find in this volume much that is useful and interesting.

EPILEPSY.

"EPILEPSY", edited by William G. Lennox, H. Houston Merritt and Thomas E. Bamford, comprises a series of papers presented at the twenty-sixth meeting of the Association for Research in Nervous and Mental Disease, held jointly with the International League Against Epilepsy, on December 13 and 14, 1946, in New York.[2] The contents have been written or supervised by prominent American neurologists, neurosurgeons and psychiatrists. There are several papers on experimental studies of cortical neuronal discharge relating to various chemicals, blood flow, muscle response, metabolism and other factors. The section on electroencephalography is of particular interest in that it reveals the intense research that has been carried out in this regard, particularly the article on "Experimental Studies on the Functional Anatomy of Petit Mal Epilepsy" by Jasper and Droogleever-Fortuyn. Medical treatment is discussed at length in several papers in relation to various modern drugs, and particularly in regard to 3-methyl 5,5-phenylethylhydantoin ("Mesantoin"). The final two sections deal with post-traumatic epilepsy resulting from wartime head wounds and the psychological-social factors related to epileptics.

It is not possible, in such a brief review, to criticize all the individual papers, or even a few of them. The book can only be summarized as an excellent collection of papers which throw a good deal of new light on to this all-important problem and bring our knowledge of the subject practically up to date. It is a book which should be added to the collection of everyone who is interested in this subject.

[1] "Blood Derivatives and Substitutes: Preparation, Storage, Administration and Clinical Results Including a Discussion of Shock, Etiology, Physiology, Pathology and Management", by Charles Stanley White, M.D., Sc.D., and Jacob Joseph Weinstein, B.S., M.D.; 1947. Baltimore: The Williams and Wilkins Company. London: Baillière, Tindall and Cox. 9" x 5½", pp. 504, with illustrations. Price: $7.50.

[2] "Epilepsy: Proceedings of the Association Held Jointly with the International League Against Epilepsy, December 13 and 14, 1946, New York"; Editorial Board: William G. Lennox, M.D., H. Houston Merritt, M.D., and Thomas E. Bamford, M.D.; Volume XXVI; 1947. Research Publications: Association for Research in Nervous and Mental Disease. Baltimore: The Williams and Wilkins Company. 9" x 5½", pp. 676, with illustrations. Price: 90s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Psychiatry in General Practice", by Melvin W. Thorner, M.D., D.Sc.; 1948. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9" x 6", pp. 680. Price: 56s.

Written "to acquaint the internist and general practitioner with those aspects of psychiatric theory and practice which are of constant daily concern to him in his professional work".

"A.M.A. Interns' Manual"; 1948. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 7" x 4", pp. 212. Price: 16s.

A manual issued by the Council on Medical Education and Hospitals and the Council on Pharmacy and Chemistry of the American Medical Association, designed for use by interns.

"The Medical Clinics of North America" (issued every two months); September, 1948. Philadelphia and London: W. B. Saunders Company, Limited. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Boston Number. 9" x 5¾", pp. 239, with illustrations. Price: £5 10s. *per annum* (cloth binding), £4 12s. 6d. per annum (paper binding).

This issue, the Boston Number, contains a symposium on specific methods of treatment; sixteen articles by various authors are included.

"Radioactive Indicators: Their Application in Biochemistry, Animal Physiology and Pathology", by George Hevesy; 1948. New York: Interscience Publishers, Incorporated. London: Interscience Publishers, Limited. 9" x 6", pp. 580, with illustrations. Price: $10.00.

Designed to offer a collective presentation of the results obtained by means of radioactive indicators.

"An Introduction to Medical Mycology", by George M. Lewis, M.D., and Mary E. Hopper, M.S.; Third Edition; 1948. Chicago: The Year Book Publishers, Incorporated. 10" x 7", pp. 392, with 103 illustrations, some of them coloured. Price: $8.50.

Intended as a "primer" in the subject. It deals with the clinical, theoretical and experimental aspects of mycology and also with laboratory procedures used in diagnosis.

"The Natural Development of the Child: A Guide for Parents, Teachers, Students, and Others", by Agatha H. Bowley, Ph.D., with a foreword by D. R. MacCalman, M.D.; Third Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 7" x 4½", pp. 214, with 84 illustrations. Price: 8s. 6d.

Intended to give an outline of the normal mental development of the child from infancy to adolescence.

"Hernia: Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis, and Treatment", by Leigh F. Watson, M.D., F.I.C.S. (Los Angeles); Third Edition; 1948. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9½" x 6½", pp. 736, with 323 illustrations. Price: £5 1s.

The latest edition of a comprehensive work, first copyrighted in 1924.

"Notes on Infant Feeding", by G. B. Fleming, B.A., M.D., F.R.C.P. (London), F.R.F.P.S., and Stanley Graham, M.D., F.R.C.P. (Edinburgh), F.R.F.P.S.; Third Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 7" x 5¼", pp. 68. Price: 3s.

Embodies the principles of infant feeding followed at the Royal Hospital for Sick Children, Glasgow.

"A Surgeon's Guide to Local Anæsthesia: A Manual of Shockless Surgery", by C. E. Corlette, M.D., Ch.M. (Sydney), F.R.A.C.S.; 1948. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8½" x 5½", pp. 372, with 200 illustrations. Price: 35s.

A surgical book "written by a surgeon, and for surgeons",

The Medical Journal of Australia

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All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

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HISTORY AND AUSTRALIAN MEDICINE.

IN the introduction to his delightful book, "The Story of Mankind", Hendrik Willem Van Loon tells Hansje and Willem, to whom the book is dedicated, how an uncle of his promised him, when he was twelve or thirteen years old, to take him on a memorable expedition. He was to be taken to the top of the tower of Old Saint Lawrence in Rotterdam. He describes how, when he entered the tower and the "mysterious door" on rusty old hinges closed behind him, he was for the first time confronted by audible silence. He and his uncle then climbed upwards; they went from one floor to the next in another of his first discoveries—tangible darkness. Then came plenty of light. After this came ladders and the tower clock and higher still the bells—the nice little bells and their terrible sisters and in the centre the big bell, seeming to reflect in solitary grandeur upon the six hundred years during which it had shared the joys and sorrows of the people of Rotterdam. In the corner all alone was the big black bell—the bell of death. Then came more ladders and suddenly the fresh air of the wide heavens and the sky above. The tower showed things in a new light—the confused commotion of the streets and the market place, of the factories and the workshop became the well-ordered expression of human energy and purpose. Then Van Loon writes that: "History is the mighty Tower of Experience, which Time has built amid the endless fields of bygone ages. It is no easy task to reach the top of this ancient structure and get the benefit of the full view. There is no elevator, but young feet are strong and it can be done". History, as we all know, gives meaning to much that is hard to understand in the present-day set-up. It has been likened to a fourth dimension and the comparison may be apt, for the fourth dimension is not defined and we may see in our historical fourth dimension more than we have just reason to see. Be that as it may, most intelligent people recognize the value of the study of history in the conduct of human affairs. Medical graduates know that the study of medicine through the ages is invaluable, nay, indispensable, if they would be worthy students of its science and exponents of its art.

If we are asked to define the scope of the history of medicine, our first reply will be to define the scope of medicine. Having declared that the study of medicine deals with the bodily and mental condition of man in health and disease and this in his relationship to his environment, we shall then say that the history of medicine deals with these aspects of human life from the time that man first tried to control and cure disease. Included in this study will be all the sciences dealing with man as a social being and in his relationship with his environment. If history is looked on as a science it must be described as mainly inductive. Facts are linked together in the order of their happening and in relation to the factors which have brought them about. If deduction is used it must be used with caution. History has been described as comprising four processes. First comes the collection of facts; secondly, there is the arrangement of those facts according to their time and cause; then comes criticism to determine the value of the facts; and finally there is the interpretation of the facts. It has also been pointed out that because the human element enters into it to such a large extent, history can never be an exact science. We can well imagine that a would-be historian with a pronounced political bias or rabid religious convictions would produce an historical account that differed considerably from what would be written by another author who was not stirred by politics or disturbed by religious dogma. An editorial in *The Times Literary Supplement* of November 13, 1948, states that the business of the historian, whether narrative or analytical, is to establish causal relations between events and that this requires precision and economy. Selection is the essence of the historian's work, for "only when he has singled out what is relevant can he give an intelligible explanation of events". Some of the difficulties of the historian are well set out in the editorial. We are told that the contemporary historian is confronted with a mass of evidence so large and varied that it is almost unmanageable. However limited the field, it will include more evidence than the historian can absorb intelligently. There is a danger that he will sit down to write with a mind charged with knowledge, but drained of inspiration. "Good history . . . is the product of a mind distinguished not by the wealth of its information but by the depth and subtlety of its understanding." If the historian is not sure of his conclusions before he begins to write and of his questions before he begins to inquire, "he can only hope to cover a pile of dead wood with a shroud of dead words".

The history of Australian medicine has yet to be written. That it is a work that should be undertaken will not be denied. The writing of history is, as we have seen, a task of some magnitude, and the man who undertakes to write the history of Australian medicine will need to have special qualifications for the work. He will also have to have a certain amount of time at his disposal. Such a person will not easily be found, but this does not mean that nothing can be done until he is discovered. There are a few historically minded practitioners in Australia and most of them are known to readers of this journal. Though they are a mere handful, their studies have been of the greatest value. Most of the studies have dealt with individuals rather than societies, associations or movements; they are none the less important on

this account, for they have shown how the practice of medicine was established and grew in the parts of the young Australia with which they have dealt. Many facts remain to be gathered before the historical work of which we dream can be carried out. As time passes and these facts are not gathered they become more and more obscure —records are lost and many sources of information are destroyed. Older people, too, whose memories and associations extend well back into the last century, are becoming fewer and fewer and soon none of them will be left. The present plea therefore is for an awakening of interest in the early days of Australian medicine. People who have to give presidential addresses, particularly to Branches of the British Medical Association and to special Groups and Sections of that body, will find in an historical subject an answer to their difficulties. The work is not easy—as Van Loon said there is no elevator—but the fascination is there and the vista from the top of the tower is more than compensation for the toil of climbing there. It is to be hoped that in the future sessions of the Australasian Medical Congress a section of medical literature will once more be included and provide a stimulus for historical research. It is curious that history has not included more medically trained persons among its devotees. History is a human study and doctors are students of man; they are also used to sifting evidence in their diagnostic studies. It may be that they have never really thought about it; the suggestion is that they should now begin.

Current Comment.

THE INTRAVENOUS ADMINISTRATION OF IRON.

FOR a number of good reasons a persistent attempt has been made to find a satisfactory means of injecting iron intravenously. Failure to elicit a therapeutic response with orally administered iron, gastro-intestinal disturbances from iron given in this way and the desire to produce a speedy effect in certain circumstances are all sound indications for parenteral administration of iron. The painful effects of its intramuscular injection have quickened efforts to find a preparation suitable to be given intravenously. Partial success has been achieved, but with little real confidence of both safety and therapeutic efficacy. Two recent reports[1] are more encouraging. In one H. G. B. Slack and John F. Wilkinson, of the department of hæmatology at the Manchester Royal Infirmary, describe their trials of many preparations over a long period and their recent success with an iron-sucrose preparation, firstly as prepared by a method devised from their long experience and secondly in a proprietary form known as "Ferrivenin". They have found no detectable difference in tolerance or response in very many batches of either of these two preparations. The scheme of dosage finally adopted was 25 milligrammes on the first day, 50 milligrammes on the second, 100 milligrammes on the third and 200 milligrammes on the fourth and subsequent days, but occasionally a dose of 200 milligrammes was given twice in a day. Only one of sixty patients developed mild reactions at the 200 milligramme level, all others tolerating this dosage well; larger single doses are not recommended. The treatment was usually completed in ten out-patient visits, or less if 200 milligramme doses were given twice daily. All of the sixty patients were suffering from iron-deficiency anæmia; the condition of ten had proved refractory to full doses of iron given by mouth over long periods. The clinical and hæmatological response was initially good in 57 out of the 60 cases and it was at times dramatic. The utilization of the iron appeared to be almost 100% and the supplementary addition of trace elements, ascorbic acid or folic acid was not apparently necessary. Utilization was, however, seriously interfered with in the presence of chronic infection.

The other report is by A. D. T. Govan and Jean M. Scott, of the Glasgow Royal Maternity and Women's Hospital, and concerns their use of "Ferrivenin" in the treatment of anæmia of pregnancy. In addition to intolerance and lack of response to oral therapy, they were confronted with the problem of severe anæmia manifesting itself only in the last weeks of pregnancy and demanding urgent treatment. They used the following general dosage scheme. During the first week injections were given daily, with an initial dose equivalent to 30 milligrammes of elemental iron on the first day, 60 milligrammes on the second day and 100 milligrammes thereafter; at the end of a week injections were reduced to 100 milligrammes on alternate days. A group of 25 patients was treated and the results were compared with those obtained when 62 patients were given iron by mouth. The difference in response was striking, not only in relation to time, but also because with the intravenous therapy succeeding increments of hæmoglobin increased, instead of diminishing, as happened with oral therapy. In all cases the intravenous therapy produced a rapid response, the hæmoglobin value increasing in almost all cases by 8% in the first week of treatment. Rapid injection of the iron preparation was found to cause venous spasm, but there was no spasm if the solution was introduced gradually. A slight and transient general reaction followed the first or second injection in about 10% of cases, but it did not occur again with further treatment. A severe reaction occurred in only one case; this appeared to be due to vagal stimulation and may have been related to irregular attendance of the patient for treatment; it was, in any case, of only a few minutes' duration and left no apparent after-effects, though further intravenous therapy was not attempted in that case. Altogether the results in this series, as in the series of Slack and Wilkinson, offer encouragement. The immediate efficacy of the therapy seems to have been demonstrated and the unsatisfactory features of earlier efforts are not apparent.

[1] *The Lancet*, January 1, 1949.

THE PROGNOSIS OF EXUDATIVE PLEURISY IN CHILDREN.

NUMBERS of surveys have been made of children and young adults with exudative pleurisy in order to assess the risk of an associated or subsequent open pulmonary tuberculosis. An editorial discussion of the subject in the *British Medical Journal* a couple of years ago drew attention to experience in the services with regard to the men who broke down after pleural effusion, and pointed out that the percentage reported in various series differed considerably, but might be somewhere in the neighbourhood of 30.[1] Perhaps useful information may be obtained later on from such studies. A recently published monograph by Herbert Nathhorst sets forth the results of a very careful investigation of children in Sweden who have had an attack of exudative pleurisy.[2] This study has been most carefully carried out. The clinical material has been chiefly drawn from Professor Wallgren's clinic in Gothenburg, and the statistical work done in the State Institute for Human Genetics and Race Biology in Uppsala. The author has had the advantage of following 471 patients treated under the control of one physician over a period of nearly twenty years, and in addition 124 children in hospitals in Stockholm were investigated. Close cooperation was maintained between the children's hospital in Gothenburg and the municipal dispensary in the following of the patients. Only those have been included who have been satisfactorily investigated by routine methods, including X-ray examination, tuberculin sensitivity tests and blood sedimentation rate estimations. Most of the children were tested by the cutaneous or percutaneous method; the author admits that a further intracutaneous

[1] *British Medical Journal*, September 7, 1946.
[2] *Acta Tuberculosea Scandinavica*, Supplement XVII, 1948.

test might have raised the already high percentage of positive results. Reaction to the tuberculin test was obtained in 585 out of 595 children. The possibility of rheumatic infection as a cause of pleural effusion was considered, but it cannot be regarded as significant in this series. Observations in the Gothenburg Children's Hospital have shown that of 689 children with rheumatic fever only 16 had pleural effusions, all but one of these being associated with pericardial effusion. Dispensary workers helped greatly in tracing former patients; the methods used were *questionnaires*, offers of gratuitous examination and personal calls.

Nathhorst's conclusions cannot be easily expressed in simple terms, for his monograph is highly statistical, in fact actuarial, in approach, and the original should be consulted for details. In it there are many points of interest. The findings in the large control series of 515 children are alone of value. It is surprising to find that demonstrable "heredity" or known exposure to risk of infection was recognized only in some 10%. The author points out that even if the relatives know of familial sources of exposure they obviously do not know of non-familial sources. Of 116 children who were found later to have pulmonary tuberculosis and about whom information was available, only fourteen were known to have been exposed to risk. It is of interest that the patients in this series lived in urban areas. The superintendent of a large city hospital in Australia once remarked when the risks of exposing young trainee nurses to tuberculosis in hospital were under discussion that the young girl coming from a more or less secluded life, especially if in the country, ran other and quite unknown risks of tuberculous infection among her intimate friends. Other topics studied are the mode of onset of the pleurisy, which was insidious in 65%, the importance of a previous history of *erythema nodosum*, and the admission diagnosis of the patients. It is significant that 84% of 160 children who had an attack of *erythema nodosum* before the onset of the pleurisy showed radiological signs of a lesion in the lung fields. With regard to the initial clinical diagnosis, it is curious that a malady so physically obvious as pleural effusion should be overlooked, even if it is stealthy in its development. Perhaps the side of the chest affected may be mentioned; it was the right side in 54·5% and the left in 45·5%, both sides being affected in some 4%. Radiologists will be cheered to know that in 466 of the 595 cases skiagrams prepared during the period of the effusion showed pathological lesions in the lung fields. During the study 112 patients were found to have clinical tuberculosis, though symptoms were not always present; 49 of these had extrapulmonary types of infection. Of 69 who had the pulmonary form, there being a few who had both types, 30 died. In all, 53 out of the 595 died later from tuberculous disease, which affected the lungs in 28 cases.

Elaborate tables have been prepared by the author to show the risks of frank tuberculous disease after a pleural effusion, relating to age, sex, time of appearance of symptoms and other factors. One of the most interesting findings which can be simply expressed is that over a period of fifteen years after an attack of pleurisy with effusion the risk of contracting tuberculosis of any form is as follows: between ages 0 and 9 years, 16%; between ages 10 and 16 years, 25%; the overall risk for all ages up to 16 years being 20%. Seeing that 78% of all patients had radiological evidence of a pulmonary lesion at the time of the pleurisy, with its possible implications concerning immunity, perhaps the end result is not so bad as it may seem. Comparisons with the control series enabled the author to determine whether the figures obtained from the patients with pleurisy were significant. For example, 6·2% of parents of children with pleural effusions died of tuberculosis, whereas the expected general rate was 3·3%.

Of course, even carefully ascertained figures such as these worked out in this research cannot be applied generally. The number of variable factors is considerable; age, race, climate, social and economic conditions all affect the risks of propinquity, and the establishment of immunity. The figures quoted in the editorial article mentioned above illustrate what divergence there is in different sets of observations, but even without an attempt to find any parallels there are many useful things to be remembered. Not the least of these is the long period of supervision which is necessary for any young person who has had a pleural effusion. This is well known, but it is not always regarded.

A NEW TREATMENT OF ALCOHOLISM.

THE non-medical Press recently published stories of a new drug which so affected the person who took it that characteristic "hang-over" effects developed immediately on the taking of alcohol. The drug is tetraethylthiuramdisulphide or "Antabuse", which has been developed by Jens Hald and Erik Jacobsen in collaboration with other workers in Copenhagen.[1] Hald and Jacobsen report that, in general, if "Antabuse" is taken at a suitable interval before alcohol, symptoms follow the taking of the alcohol mainly involving the circulatory and respiratory systems. They include intense superficial vasodilatation involving the face and sometimes spreading further, dilatation of the scleral vessels, a little later palpitations and sometimes dyspnœa, and with larger doses nausea and vomiting with pallor; an accompanying headache is usual. The symptoms are very unpleasant, but disappear within a few hours, generally leaving the person rather sleepy. The characteristic effect of alcohol does not appear unless the "Antabuse" is taken at least three hours earlier; in some clinical trials this latent period was as long as forty-eight hours. The effective doses of the drug appear to produce no effect whatever if no alcohol is taken, and so far animal experiments and clinical observations have revealed no evidence of significant toxic effects. The mode of action is by no means clear. The symptoms can be fully explained by an increased formation of acetaldehyde which occurs after the taking of alcohol by persons previously treated with "Antabuse". but why the acetaldehyde is formed has yet to be explained. Hald and Jackson discuss the point in their paper and give other pharmacological data about the drug.

The clinical effects of "Antabuse" are described in a separate paper by O. Martensen-Larsen, who at the time of recording his work had been using the drug for about six months. He stresses the fact that the period of use is too short to permit full assessment, but he seems to be justified in considering his results "promising". This is his scheme of treatment:

> After careful physical examination and study of the medical, psychiatric, and social background, the patient is given 1·0-1·5 g. of antabuse and is told to continue with 0·5 g. daily. He is told that he will become ill if he drinks alcohol, and is asked to return for a second interview two or three days later. The patient takes two or three drinks either the night before or immediately before the second interview to show the effect of the treatment. . . . A few patients, mostly heavy drinkers, can take considerable amounts of alcohol before the effect appears. In such cases the medication is continued and the patient is tested in the same way at intervals of four to six days. The tolerance for alcohol is, however, gradually reduced.

Martensen-Larsen has treated 83 patients, 25 of them for from four to seven months, the rest for shorter periods. All alcoholics who have consulted him have been given the treatment without selection. There have been nine failures, most of the subjects having serious psychic defects; in every case "Antabuse" produced its characteristic effects, but the patients lacked interest and refused to continue treatment. Further analysis of results and three illustrative case histories are given in the paper, but as a general statement 74 patients appeared to receive benefit ranging from apparently complete cure to control while they could be persuaded to persist with treatment. The follow-up is, as Martensen-Larsen points out, too short to indicate how long the results will last, or if any undesirable side-effects will follow the protracted use of "Antabuse". For this reason caution is advised in the treatment of patients with organic diseases. Moreover, especially in severe cases, other forms of treatment such as psychotherapy may still be needed.

[1] *The Lancet*, December 25, 1948.

Abstracts from Medical Literature.

PHYSIOLOGY.

Renal Arterio-Venous Anastomoses.

B. SIMKIN *et alii* (*Archives of Internal Medicine*, February, 1948) have injected minute glass spheres of known size into the renal arteries of normal human kidneys *post mortem*, and have demonstrated the existence of arterio-venous anastomoses by recovering from the renal vein spheres with diameters many times greater than the average diameter of a capillary blood vessel. The mixture injected consisted of two grammes of the glass spheres (six million of which go to the gramme) suspended in 100 millilitres of a gelatin, heated to 40° C. so as to be fluid. The spheres recovered measured from 90μ to 440μ in diameter. These large spheres were recovered from the renal veins of kidneys with and without intact capsules, which showed that arterio-venous anastomoses were present in the body of the decapsulated kidney. The existence of arterio-venous anastomoses during life was demonstrated by the injection of glass spheres into renal arteries of living anæsthetized rabbits and dogs and the recovery of spheres measuring 50μ to 180μ in diameter from the venous circulation. The authors suggest that the anastomoses function and have a physiological significance during life.

Distribution of Sympathetic Fibres in the Brachial Plexus.

S. SUNDERLAND (*Brain*, March, 1948) describes the distribution of the sympathetic fibres in the brachial plexus with particular reference to their possible implication in the production of vascular complications in cases of cervical rib. The observations were made on normal dissecting-room and post-mortem material and on the brachial plexus of a patient with a cervical rib, in whom vascular symptoms were the predominating clinical feature during life. The investigation revealed no anatomical peculiarities about the distribution of the sympathetic fibres in the plexus which would have exposed them more than their somatic neighbours to irritation or pressure by the cervical rib. The findings, however, do not exclude the possibility that mechanical stimulation of a few of the scattered sympathetic components in the lower trunk, or of the periarterial sympathetic plexus about the subclavian artery, may set up a source of chronic irritation at the site of stimulation which might excite widespread vascular effects at the periphery with the production of vascular symptoms. When this occurs in the absence of impairment of somatic motor and sensory function, it must be assumed that the sympathetic components are physiologically more susceptible to stimulation than the somatic components around them.

Nutritional Deficiencies and Greying of Hair.

D. V. FROST (*Physiological Reviews*, July, 1948) states that the fact that greying has been induced in all species of animals studied and has been observed in human infants under a variety of dietary deficiency conditions would seem to indicate that greying, particularly during growth, is a characteristic manifestation of certain types of dietary deficiency. The intent in most experiments has been to develop a specific deficiency of only one pigmentation factor. Such extreme specific dietary imbalances are rare among humans, but multiple deficiencies do occur. That greying is ever actually induced under ordinary conditions by mild chronic deficiencies of various *B*-complex and mineral elements has not been proved. Since genetic, hormonal and dietary influences have all been shown to play a part in pigmentation processes, the ætiology of greying in individual people is unavoidably obscure. The practice of ascribing human curative or prophylactic properties to single pigmentation factors, found effective in animals under special conditions, is not well founded. It is not certain that greying in human adults is ever caused by a dietary deficiency, and, if this was so, the deficiency would almost certainly involve the lack of more than one of the factors so far shown to be needed for normal pigmentation in animals. The author considers that, because of genetic influences, greying in adult human beings is not a manifestation of unnatural physiological change. The fact that greying occurs in children on extremely poor diets is of interest, but it helps little in assessing the situation with regard to adults. The author explains that the work with human beings on which these statements are based was carried out before the need for pteroylglutamic acid for normal pigmentation was established in animals. Most of the human studies involved pantothenic acid. He considers it of interest therefore that there now appears to be physiological relationship between these factors. The apparent functional relationship between pteroylglutamic acid and the liver principle concerned with pernicious anæmia is also of interest, particularly as liver extract is reputed to have an effect on greying in isolated instances.

Brain Metabolism.

D. RICHTER AND R. M. C. DAWSON (*The American Journal of Physiology*, July, 1948) state that the lactic acid content of the rat brain is reduced during sleep and increased during emotional excitement. The rise in the lactic acid content of the brain during emotion is not due to concomitant muscular activity, since the effect was still observed in animals immobilized by tubocurarine. The brain lactic acid content was not raised by muscular exercise in trained animals. The rise in lactic acid content of the brain during emotion is a transient effect, followed by a rapid return to normal when the stimulus is discontinued.

Salt Excretion in Desert Mammals.

K. SCHMIDT-NIELSEN, B. SCHMIDT-NIELSEN AND H. SCHNEIDERMAN (*The American Journal of Physiology*, July, 1948) state that some desert rodents excrete very concentrated urine, which enables them to expend only small amounts of water for excretion purposes. The authors carried out investigations of the excretory ability of the kangaroo rat and the pocket mouse, which can live indefinitely without drinking water and gain weight on a diet of dry grain only; for test purposes the animals were given grain containing 10% by weight of sodium chloride. The maximum excretory ability with respect to electrolytes and to chlorides appeared to be far in excess of the limits known from other mammals. The authors consider that this ability must be interpreted as a very useful mechanism for water conservation and an adaptation to desert life.

Cerebral Ischæmia and Hypertension.

A. C. GUYTON (*The American Journal of Physiology*, July, 1948) states that a considerable rise in blood pressure occurs in response to acute cerebral ischæmia. This response is still present after reflexes from the carotid sinuses have been abolished. Quantitative data indicate the cerebral pressoreceptor response to be as powerful as the carotid sinus response, though of a slightly different character. Respiration is also depressed by acute cerebral ischæmia, and the rise in blood pressure generally is greatest when the respiration is barely present. Prolonged cerebral ischæmia produces complete medullary paralysis causing the blood pressure to fall to levels of a spinal animal. It is postulated that the centres responsible for the blood pressure response are located in the medulla. The blood pressure response due to cerebral ischæmia is almost identical with that shown by Cushing to occur in association with increased cerebro-spinal fluid pressure. The possible relationship of these observations to essential hypertension is discussed.

Shock due to Electrical Injury in Frogs.

L. MOREAU, M. BALISTOCKY AND L. V. HEILBRUNN (*The American Journal of Physiology*, July, 1948) have produced profound physiological depression and death in the frog by means of suitable doses of electrical injury applied to either the brain or hind legs. Evidence of a circulating toxic factor was seen in the fact that the toxic effects were prevented by interruption of the blood circulation. Disturbances in the blood-clotting mechanism following injury indicate that the toxic factor is a substance, or a group of substances, with thromboplastic properties. These results favour the concept that thromboplastic substances may be involved in the pathogenesis of shock.

Mode of Secretion in the Parathyreoid.

S. H. BENSLEY (*The Anatomical Record*, July, 1947) states that in many glands the cytological changes associated with the process of secretion have been elucidated. In the parathyreoid gland, however, evidences of secretory activity, at least as regards the nature of the intracellular antecedents of secretion, have not been clearly defined, so that at present it is difficult to state from the examination of the parathyreoid gland whether the gland was elaborating, exporting, or storing the secretory products. Many different structures and substances have been described as possible antecedents of secretion in the parathyreoid cell, and many different cell types have been differentiated as possible stages in the activity of the secretory cell. The author proposes that there are at least four phases in the secretory cycle of the parathyreoid cell: the resting phase, the phase of hylogenesis, the phase of export, and the storage phase; and that these phases may be

correlated with the character and distribution of the cellular constituents. These constituents can best be preserved by a mixture of redistilled neutral formalin, Zenker base and osmic acid, and can best be visualized, when certain precautions are taken, by being stained with aniline acid fuchsin, phosphotungstic acid and methyl green. With this cytological method there appear to be three forms of secretory antecedent in the cells of the parathyreoids of the dog: pale staining vacuoles, colloid, and stainable bodies which differ from each other in density. The vacuoles and colloid appear to be related to a higher fluid content of the cell and perhaps to more rapid synthesis; the denser stainable bodies seem to be related to a lower fluid content and perhaps to a slower synthesis. Reduction in parathyreoid tissue produced moderate hyperplasia, cellular hypertrophy, and increase in the secretory activity in the remaining glands. In some cases the injection of sodium oxalate, presumably by lowering the blood ionic calcium level, produced further cellular hypertrophy and increase in the secretory activity in the parathyreoids of parathyreoprival dogs. The response, however, was so varied in the dogs that it seems likely that either the action of sodium oxalate was more complex than a direct stimulus to the parathyreoid or else other unrecognized factors (such as diet, excretion, rate of calcium mobilization *et cetera*) complicated the reaction.

BIOCHEMISTRY.

Vitamin Deficiencies and Metabolism.

R. E. OLSON *et alii* (*The Journal of Biological Chemistry*, September, 1948) report that the oxygen consumption of heart ventricle slices without added substrate is not affected by thiamine deficiency in ducks, but is increased by thiamine deficiency in rats. The oxygen consumption of heart ventricle slices with added pyruvate is decreased by thiamine deficiency in ducks, but is unaffected by thiamine deficiency in rats. The rate of pyruvate disappearance in heart ventricle and the rate of its conversion to non-lactate products are decreased by thiamine deficiency in both species. The addition of thiamine *in vitro* to heart ventricle slices from deficient ducks increases both the oxygen consumption and the pyruvate disappearance. The rate of pyruvate utilization in duck ventricle increases with the thiamine content up to a level of 2·5γ per gramme of fresh ventricle. Further increases in thiamine content have no further effect upon pyruvate utilization. A comparison of the rates of lactate accumulation with and without added pyruvate in normal and thiamine-deficient rats and ducks would indicate that inanition is more effective in increasing lactate formation than is thiamine deficiency. The depression in oxygen consumption of auricular muscle seen in thiamine-deficient rats was not observed in thiamine-deficient ducks. An explanation for this species difference is suggested.

R. E. OLSON *et alii* (*ibidem*) have found that the oxygen consumption of heart ventricle slices from biotin-deficient ducks in the presence and absence of pyruvate and in the presence of succinate is decreased 35%, 43% and 28% respectively from that of ventricle slices from pair-fed normal controls. The values for ventricle from controls fed *ad libitum* were not significantly different from those of the pair-fed controls. The accumulation of lactate in ventricle slices from biotin-deficient ducks in the presence and absence of pyruvate was decreased to about 20% of the values from pair-fed controls and to about 45% of those from controls fed *ad libitum*. The higher lactate formation in pair-fed ducks appeared to be related to their state of partial inanition. The conversion of pyruvate to non-lactate products was reduced 48% in ventricle slices from biotin-deficient ducks. Production of $C^{14}O_2$ from carboxyl labelled succinate in heart ventricle from biotin-deficient ducks was decreased 55% from that of pair-fed controls. The prior intraperitoneal administration of biotin to deficient ducks restored the respiration and pyruvate utilization of heart ventricle slices essentially to normal. The incubation of deficient heart ventricle slices with biotin *in vitro* had no significant effect upon their respiration or pyruvate utilization. The respiration and pyruvate utilization of auricular and ventricular heart muscle, in general, were depressed to the same extent in biotin-deficient ducks.

Pantothenic Acid Deficiency.

R. E. OLSON AND N. O. KAPLAN (*The Journal of Biological Chemistry*, September, 1948) have found that rats maintained on diets lacking pantothenic acid for periods up to nine weeks maintain normal content of coenzyme *A* in their tissues for two to three weeks and then show a gradual depletion to a level 35% to 40% of normal. Ducklings show a rapid depletion of coenzyme *A* in their tissues, to 40% of normal, when placed upon a diet deficient in pantothenic acid. Liver slices from rats and ducks deficient in pantothenic acid have a decreased ability to utilize pyruvate. This accompanies a low content of coenzyme *A*. Injection of pantothenate into deficient ducks results in a large increase in coenzyme *A* in the liver and increases the ability of surviving liver slices to utilize pyruvate. The addition of pantothenate to heart and liver slices from deficient ducks results in small but definite increases of coenzyme *A* (of the order of 30%). Normal slices do not synthesize additional coenzyme *A* under these conditions. Added coenzyme *A* and its cleavage products do not increase the coenzyme *A* synthesis in deficient tissue slices any more than their respective full pantothenic acid equivalents. Nitrogen, arsenite, and glucose interfere with the synthesis of coenzyme *A in vitro*.

Carbonic Anhydrase.

W. ASHBY AND E. BUTLER (*The Journal of Biological Chemistry*, August, 1948) report that study of the distribution of carbonic anhydrase in the central nervous system with development of the normal fœtus of cattle has indicated the following: (i) a progressive caudal to rostral increase in the enzyme approaching the adult pattern; (ii) in contrast to other enzymes studied in the fœtal central nervous system, an absence of the enzyme from the cerebrum until late in fœtal development; (iii) from the seventh month to birth, except for its absence in the pallium, a clean-cut repetition of the pattern of relative content of the enzyme with an approach in magnitude to the level found in the adult. An early appearance of the enzyme was found in the blood of fœtal cattle, in contrast to the finding of other investigators for fœtal goats. In the human premature and full-term infants the data indicate the following: (i) a caudal to rostral increase in the enzyme with increase in menstrual age; (ii) a less complete approach to the adult pattern of distribution in the full-term infant than in the six-month cattle fœtus; (iii) no carbonic anhydrase in the cerebrum at birth. The possibility is considered that the absence of carbonic anhydrase from the cerebrum of the full-term human infant may be abnormal.

Desoxycorticosterone.

D. M. GREEN (*The Journal of Laboratory and Clinical Medicine*, July, 1948) has found that the immediate effect of desoxycorticosterone acetate (DCA) implantation in young rats maintained on isotonic saline solution was a rise in fluid intake. The more delayed responses to the drug included a secondary regression of intake values toward control levels and the reciprocal development of hypertension. The degree of hypertension which developed appeared proportional to the dosage of the drug, the maximal rise in fluid intake, and the subsequent rate of decline in intake. No evidence was found that adrenalectomy sensitized the test animals to the actions of desoxycorticosterone. The possibility is suggested that the hypertension induced by desoxycorticosterone overdosage may not represent a direct action, but may be a compensatory mechanism for overcoming distortions in fluid and electrolyte balance produced by the drug.

MEDICINE.

Prediction of Huntington's Chorea.

R. M. PATTERSON, B. K. BAGCHI AND A. TEST (*The American Journal of Psychiatry*, June, 1948) state that 26 offspring representatives of nine families with Huntington's chorea in the immediate ancestry were subjected to physical, neurological, psychiatric, psychometric, anthropometric, genetic and electroencephalographic investigation. Of these various procedures, but two seemed to offer probable predictive value, namely, electroencephalography and blood grouping. Nineteen of the subjects showed definite electroencephalographic abnormalities, particularly in the motor regions. No definite intrafamily, interfamily or parent-offspring electroencephalographic resemblances were noted. The study of blood grouping was expanded to include all available cases of Huntington's chorea in addition to the offspring study and disclosed a disproportionately large number of individuals in groups A and O. Long-range follow-ups with repeated electroencephalographic examinations of a larger series of offspring are recommended, as well as a much more extensive examination of the blood groupings of subjects of Huntington's chorea and their offspring, in order to establish the statistical validity of the two procedures.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on November 18, 1948, at Broughton Hall Psychiatric Clinic, Leichhardt. The meeting took the form of a series of clinical demonstrations and was arranged by DR. GUY LAWRENCE, the medical superintendent of the clinic. Parts of this report appeared in the issues of January 8 and 22, 1949.

The Rorschach Test.

Dr. Barrow, the honorary psychologist to the clinic, discussed the Rorschach test, which was, he stated, in the words of its founder, "a method of personality diagnosis". A Swiss psychiatrist, Herman Rorschach, had chosen empirically ten ink blots from a large number, using as a criterion their lack of content, the theory being that the subject must project himself into an interpretation of the blot. The tester was interested in several things: (i) what the patient saw in the blots; (ii) whether the images were taken from the whole or parts of the blots; (iii) whether colour, movement, shading or some other factor had helped to determine the response; (iv) whether the contents of the responses were human, animal, sexual, abstract *et cetera*; (v) the times taken for each card. Dr. Barrow said that the test had become a useful diagnostic tool, for the responses formed specific constellations, which helped in the establishment of the nature of the mental abnormality. For example, schizophrenic records consistently illustrated the tendency to misunderstand reality in the subjects' irrelevant generalities. Apathy and indifference to situations also were shown in the lack of constructiveness throughout the tests, the records usually revealing a confused sequence of responses. Perhaps the most common characteristic, however, in the Rorschach scoring of schizophrenia was found in the marked inequality of responses from card to card. It was not uncommon to find exceptionally good reactions side by side with others which were poor, low grade, crude and completely irrelevant.

Korsakow's Psychosis.

A male patient, aged fifty-seven years, with Korsakow's psychosis, was shown. He had been drinking excessive amounts of alcohol since his wife died two and a half years previously. For two or three months he had been dull and apathetic. He confabulated freely, was disorientated for time and place and had a very bad memory. Signs of severe peripheral neuritis were found on examination. It was pointed out that there were two factors in the production of such a condition—namely, the toxic action of alcohol and avitaminosis. *Delirium tremens* probably occurred when there was a sudden deficit of vitamin B_1 complex, due either to anorexia or to vomiting or to both. If the avitaminosis reached a certain degree of intensity the delirium did not resolve in the usual two or three days, but passed into a subacute or chronic confusional state, which, if associated with polyneuritis, as in the case under discussion, constituted Korsakow's syndrome. The treatment consisted of sedation with paraldehyde; bromides and other toxic sedatives should be avoided. Large doses of vitamin *B* were given, the appetite was stimulated with insulin, and vitamins were supplied parenterally as well as by mouth.

Drug Addiction: Chloral Hydrate.

A male artist, aged forty-six years, had been interested in his chosen profession since childhood to the exclusion of other studies. He engaged in little sport, but liked boating, was a member of a life-saving club and was fond of men and women. He served for thirteen years as a humorous artist and cartoonist on a newspaper staff, then broke off an engagement and went roving in the Pacific Islands. In 1935, after a long walk in the sun, and after a particularly heavy bout of smoking, while lying down in his bungalow at Tahiti, he developed a very severe headache and also an acute anxiety state. He ran wildly down the road and was put into hospital at Papeete, being told that he had sunstroke. Fearful of going mad, he "panicked". Developing insomnia, he began to take "Bromural" up to as many as 25 tablets a night, and became an addict. As well, he took alcohol and smoked to great excess. He developed excessive fears of insomnia and became introverted. After treatment at Broughton Hall in 1939 for acute anxiety state and drug addiction, he made a fair recovery, but it did not last long. Psychoanalysis in 1941 was unsuccessful. He was readmitted to Broughton Hall in September, 1948, having been working at his art and having been kept going chiefly by daily doses of "Dormol"; the dose had been increased from two to three ounces to six to eight ounces daily, with the addition of some "Luminal" tablets. He was anxious and feared insanity, thinking that he might become violent. He feared noises and did not desire company. Acutely depressed and unable to sleep, he wept frequently. Physically he was extremely emaciated and had a most unhealthy appearance. His blood pressure was raised and his pulse rate was comparatively slow. The arteries were palpable and tortuous. A coarse tremor of all parts of the body was present, and the tendon reflexes were much increased. His teeth were loose and inclined to fall out, and he was not eating and had no desire to eat. His pupils were equal and reacted slowly to light, but the consensual and accommodation reactions were normal. The treatment given included vitamin B_1 in large doses parenterally, especially nutritious and easily digested food, aperients and prolonged rest and massage. It was explained that "Dormol" was a proprietary preparation which contained about 25 grains of chloral hydrate to the ounce. The psychoanalysts held that the basis of drug addiction was in a narcissistic or homosexual reaction, which was no doubt more obvious in alcoholics. That basis should be exposed by analysis after the patient had been rendered free from the effects of the drug.

Puerperal Psychoses.

As an introduction to the presentation of a series of patients suffering from puerperal psychoses, it was pointed out that pregnancy, parturition and lactation presented a combination of physical and psychological stresses which frequently precipitated acute psychoneurotic and psychotic reactions. In the class of case referred to there need be no obstetric complications; the patient was often a *primpara* and of immature personality, with over-conscientious trends. Some young mothers were overwhelmed by the responsibility of caring for their babies. They had no confidence in themselves, and were the victims to some extent of the instruction they received, for they thought that if everything was not done according to rule the baby would suffer. They became anxious, and sometimes the anxiety led to acute depressive or confusional states. Although the prognosis in those cases was good, the duration of illness was rather prolonged, and it might take many months for recovery to take place if ordinary methods of treatment were used. Convulsant shock therapy had proved to be of the greatest value for patients in these states, and a favourable response was seen usually within a fortnight, with recovery within two to three months. The treatment was combined with rest, tonics, good food and explanatory discussion as was appropriate. The first patient presented had had a poor early life, and since marriage a most unhappy domestic experience. She had to work because her husband refused to keep her, and sexual relations were very unsatisfactory. After the birth of her last child she felt inadequate, and became confused and then excited and elated. Hallucinations developed, with disorientation, restlessness and destructiveness. However, she was not suicidal, and signed the voluntary admission form. Physically she was found to be undernourished. She was obviously exhausted after the confinement, and it was considered that that fact, added to the unhappy background, had set free the underlying train of mental symptoms.

The second patient had a family history of nervous instability and had had a most unhappy childhood. After marriage at the age of twenty-two years she always felt inferior to her husband; she desired pregnancy, and was worried over non-conception. However, a baby was finally born uneventfully. Before the birth she worried lest the baby should be dead, and after the birth worried excessively, blaming herself because the baby would not take the breast. A month later she said that her clothes were constantly dirty, developed a confusional state and had to enter a mental hospital. She responded to electroconvulsive therapy and went home in three months' time. A week later she became depressed and received more treatment. When first admitted to Broughton Hall she was dull and retarded, lacked interest and had an impaired memory for events preceding the illness. She felt inferior and depressed, thinking that she might commit suicide. Her physical condition was poor from lack of food.

The childhood and married life of the third patient were quite happy, and she was well until her third baby was born. A course of 23 treatments with electroconvulsive therapy was given in a private hospital, where she developed evidence of a manic-depressive state. On her arrival at Broughton Hall she was confused and restless, disorientated and over-resistive. However, she had more lucid intervals, when she was deeply depressed and emotional. Hallucinations of voices were present, and she also had an idea that her fingers varied in size from very big to very small. She

insisted that she was about to die of her manifold illnesses and was not cooperative. Her physical condition was poor. Treatment consisted of extra food and sedation, electroconvulsive therapy and explanatory discussions. It was noted that she desired to have the last baby, which she said would give her amusement and company when the other children, who were already in their teens, were away.

The last patient, a woman, aged forty-one years, shortly after the birth of her fifth child began to talk foolishly, making absurd statements regarding her husband and children. She was worried about being unable to feed the baby on the breast, and felt inadequate to cope with the situation. She had hallucinations of hearing voices, and felt that people wanted to harm her and talked about her. She showed lack of interest, severe depression and muteness, and was not cooperative in the ward when examined. It was considered that bodily exhaustion was an important factor in her condition.

Depressive States.

Three patients were presented as examples of the depressive state. The first, a man, aged fifty-eight years, with a poor heredity, at first developed an anxiety state, probably induced by sex abstinence, and accentuated by his knowledge that an electrocardiogram showed evidence of coronary sclerosis. More recently, in his involutional years, he had become depressed. The outlook was poor, and the risk of suicide considerable. It was thought that he might pass into a psychotic state. He was being treated with insulin in small doses and a diet rich in vitamins. Electroconvulsive therapy had failed to alleviate his condition.

The other two patients were diabetics. One had had an unhappy marriage, had experienced an artificial menopause, and had finally developed symptoms of conversion hysteria after she had been nearly responsible for a serious accident. She heard voices and had attempted to commit suicide. Signs of diabetic polyneuritis were also present, and it was considered that all the various factors had combined to build up serious mental disease. The other diabetic had discovered her condition only ten years earlier, when she was aged fifty-one years. About seven years later she had a mild transient depressive attack and recently had become depressed and apathetic, believing that people were talking about her. Although she spoke about suicide, she had made no active attempts in that direction.

Subacute Combined Degeneration.

A woman, aged forty-three years, had begun to complain seven years before her admission to hospital of tingling and numbness in the arms, with an aching pain in each leg; unsteadiness of gait, increased when she shut her eyes, gradually developed into severe ataxia. The calves of her legs were tender on pressure, and her legs were weak and spastic. Her mind was quite clear, but she seemed to be unduly cheerful. There were loss of vision in the right eye, paresis of the right abducent nerve and transient diplopia. The pupillary reactions were usually normal, but not always. Her general sensory functions were intact, but hyperalgesia followed deep pressure over the calves. The patient had a very ataxic gait, brisk tendon reflexes, hypertonus of muscles, bilateral extensor responses to plantar stimulation and no abdominal reflexes. There was loss of power in both arms, with tingling in the fingers. A moderate degree of anæmia was present, suggesive of pernicious anæmia in the early stages. Achlorhydria was complete. Treatment was instituted with liver extract, hydrochloric acid, vitamin B_1 and massage. The pernicious anæmia was controlled, the right leg apparently remained in a chronic residual state of spasticity and weakness, but the left leg showed signs of increased activity of the disease process. The left knee jerk was more active than the right, and the neuritis was more painful. It was pointed out that in all cases of subacute combined degeneration of the spinal cord the dorsal and lateral columns were affected in varying degrees and the peripheral nerves were involved. The almost constant presence of tenderness in the calf and plantar muscles—a tenderness not encountered in any other disease of the cord—was held by Walshe to be of diagnostic value. The principal features in the case under discussion were the progressive degeneration of the peripheral nerves, of the dorsal columns and of the lateral columns, the presence of achlorhydria and the initially high colour index of the blood.

Presenile Dementia.

An unmarried dredge fireman, aged fifty-eight years, had begun to have severe headaches two and a half years before his admission to hospital, with absent-mindedness, restlessness, forgetfulness and impairment of perception. He could give no coherent account of himself and was disorientated for time and place, but at times he was correct in his statements. Simple mental tests were beyond him. Later the headaches ceased, but the degree of dementia increased. Examination revealed no serological evidence of syphilis in the blood or cerebro-spinal fluid, and the cerebro-spinal fluid was not under pressure. His arteries were a little hardened, but there was no outstanding increase in blood pressure. The chief causes of dementia appearing in the sixth decade were stated to be neurosyphilis, cerebral tumor, vascular lesions and presenile dementia. In the case under discussion general paralysis of the insane could be excluded by the absence of appropriate serological reactions, tumour by the absence of any evidence of raised intracranial pressure, and vascular lesions by the gradual progression of symptoms without dramatic episodes. Presenile dementia remained, and the patient's condition conformed to Alzheimer's variety of that type of cerebral degeneration. The patient was in the correct age group; the aphasic and apraxic symptoms associated with dementia, the memory defects and failure of orientation were appropriate; he was restless and futile. The prognosis was hopeless. Patients in that condition might advance to a state of great dementia; then fits and coma might supervene and death follow from exhaustion.

Medical Societies.

A MEETING of the Medical Sciences Club of South Australia was held on July 2, 1948, at the Institute of Medical and Veterinary Science, Adelaide.

The Significance of Action Potentials in Nerve and Muscle.

DR. M. H. DRAPER discussed the significance of action potentials in nerve and muscle. He said that biological potentials were only readings of a rather sensitive meter. Those readings as such had no meaning; the meaning had to be supplied by the investigator from his knowledge of the situation from which the potential differences were being measured. The potential differences which concerned a neurophysiologist were both small and rapidly changing. For their measurement a complex array of apparatus was needed, but the principle was unchanged—two points of the system to be investigated were connected to the meter and a reading was taken. Cathode ray recording was the most suitable, but for that a potential difference of the order of tens of volts was needed to deflect the beam of electrons. The action potentials of nerve and muscle were much smaller, and so an electronic amplifier was needed to amplify from about ten microvolts to the required deflection voltage. The only limit in that system to the faithful recording of rapid potential changes was the amplifier, which should have a suitable frequency response. If two hypodermic needles, insulated to their tips, were placed in the belly of a muscle (for example, in the forearm) and the potential changes accompanying various degrees of contraction of the muscle were observed, a number of observations could be made. Firstly, when the muscle was at rest, so was the trace on the cathode ray tube. Secondly, with slight activity a number of characteristic spikes appeared on the screen. Thirdly, with increased activity the trace assumed a complex form, and it was difficult to pick out any spike elements. If instead of two needles in the muscle two pads were placed on the skin over the muscle, the same observations could be repeated, except that then it was difficult to say from the record what components were present. With certain degrees of contraction a quasi-sinusoidal wave form could be obtained, similar to the electroencephalographic records of α rhythm. Thus, if the muscle was used as a comparatively simple generator of spike potentials, it was possible to study the way in which many thousands of spike potentials were added together and to observe the capacitative effect of the skin in smoothing out the record. Recordings from nerve fibres had shown that nervous activity was also accompanied by spike potentials. They were smaller and more rapidly changing than those in the muscle. Therefore, since it was known that the central nervous system must be in receipt of many thousands of action potentials per second, if the gross record of the potential changes of the brain between any two points on the scalp was examined, potential changes were found of sufficient rapidity (allowance being made for the capacitative effect of the skin) to lend support to the thesis that some components of the electroencephalogram were similar to the action potentials of the nerve. In lesions of the cortex the spike components of the electroencephalogram could become pronounced.

Dr. Draper said that if the various theories concerning the origin and role of the action potential were examined, there was no uniformity of opinion. In recent years there had been interesting developments concerning the macromolecular structure of the muscle fibres. It had been shown that a single element of the muscle fibril was a most complex structure. On the biochemical side more knowledge of the proteins involved in the contractile process had appeared. Even with that more detailed knowledge—still far from complete—it was clear that in the case of muscle there was still no satisfactory understanding of the action potential. In the case of nerve, no such detailed knowledge was available. Thus understanding of the significance and role of the action potential of nerve lacked even the basis for speculation.

Carotene Metabolism.

MR. P. A. TRUDINGER discussed carotene metabolism. He said that crytoxanthin appeared to have a biological function in the hen other than its conversion to vitamin *A*. In rats, storage of vitamin *A* produced by various carotene isomers varied according to the growth-promoting powers of all except α-carotene, which might be used metabolically *per se*. Rats fed on a diet deficient in vitamin *A* and carotene, but supplemented with vitamin *A*, stored significant amounts of β-carotene. There seemed to be a carotene threshold in the rat liver, no vitamin *A* being stored until that level was reached. On the contrary, vitamin *A* was utilized for the synthesis of carotene to maintain that level when carotene supplies were deficient. The relatively high concentration of carotene in the testes, and comparison with lower forms of life, indicated that carotene might take part in reproductive metabolism.

Australian Medical Board Proceedings.

QUEENSLAND.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Acts, 1939 to 1946*, of Queensland, as duly qualified medical practitioners.

Joyce, Brain Bilbrough, M.B., B.S., 1943 (Univ. Sydney), Mines Side, Mount Isa.

Dooley, Desmond James, M.B., B.S., 1947 (Univ. Melbourne), c.o. Mr. K. Ryan, 231 Kent Street, Teneriffe, Brisbane.

O'Reilly, Merrick John Justyn, M.B., B.S., 1939 (Univ. Sydney), c.o. Department of Public Health, William Street, Brisbane.

Archos, Keith Platon, M.B., B.S., 1948 (Univ. Queensland), 37 Ninth Avenue, Coorparoo, Brisbane.

Burns, Douglas Forsyth, M.B., B.S., 1948 (Univ. Queensland), Macquarie Street, St. Lucia, Brisbane.

Cavaye, Graham Bell, M.B., B.S., 1948 (Univ. Queensland), 1 Park Road West, Highgate Hill, Brisbane.

Davison, Alan, M.B., B.S., 1948 (Univ. Queenslend), 257 Enoggera Road, Newmarket, Brisbane.

Douglas, Gavin James, M.B., B.S., 1948 (Univ. Queensland), 17 Sutherland Avenue, Ascot, Brisbane.

Anderson, Joan Blandford, M.B., B.S., 1948 (Univ. Queensland), c.o. Dr. P. A. Earnshaw, Drane Street, Clayfield, Brisbane.

Gairns, Shirley Roy, M.B., B.S., 1948 (Univ. Queensland), King's College, Kangaroo Point, Brisbane.

Gallagher, Maurice John, M.B., B.S., 1948 (Univ. Queensland), 37 Gordon Street, Mackay.

Hodges, Douglas James, M.B., B.S., 1948 (Univ. Queensland), c.o. T. Lynn, Esq., Jardine Street, Kedron, Brisbane.

Hood, Jessie Lurleen, M.B., B.S., 1948 (Univ. Queensland), McLeod Street, Herston, Brisbane.

Horn, Marie Laura, M.B., B.S., 1948 (Univ. Queensland), "Monomeet", Enoggera Terrace, Paddington, Brisbane.

Jacklin, Desmond John, M.B., B.S., 1948 (Univ. Queensland), St. Leo's College, Wickham Terrace, Brisbane.

Kelly, Patrick Dermott, M.B., B.S., 1948 (Univ. Queensland), 356 Milton Road, Auchenflower, Brisbane.

Lee, John Francis, M.B., B.S., 1948 (Univ. Queensland), 214 Cavendish Road, Coorparoo, Brisbane.

Lowth, Lawrence John, M.B., B.S., 1948 (Univ. Queensland), St. Leo's College, Wickham Terrace, Brisbane.

Lulham, Clifford Robert, M.B., B.S., 1948 (Univ. Queensland), 381, Milton Road, Auchenflower, Brisbane.

Mellick, Selim Abraham, M.B., B.S., 1948 (Univ. Queensland), St. John's College, Kangaroo Point, Brisbane.

Mitchell, Paul Wanostrocht, junior, M.B., B.S., 1948 (Univ. Queensland), "Grangehill", Gregory Terrace, Brisbane.

O'Connor, Anne Mary, M.B., B.S. (Univ. Queensland), 158 Gympie Road, Kedron, Brisbane.

Powell, Owen Watkins, M.B., B.S., 1948 (Univ. Queensland), Briggs Road, Taringa, Brisbane.

Price, Henry Michael, M.B., B.S., 1948 (Univ. Queensland), 537 Sandgate Road, Clayfield, Brisbane.

Stevens, Samuel Roscoe, M.B., B.S., 1948 (Univ. Queensland), 19 Terrace Street, Paddington, Brisbane.

Sullivan, John Joseph, M.B., B.S., 1948 (Univ. Queensland), "Oakton", Herston Road, Herston, Brisbane.

Tennant, James Neil, M.B., B.S., 1948 (Univ. Queensland), "Cairnbroe", Stafford Street, Clayfield, Brisbane.

Trotter, Laurie, M.B., B.S., 1948 (Univ. Queensland), Horatio Street, Annerley, Brisbane.

Watson, James Richard Henry, M.B., B.S., 1948 (Univ. Queensland), School Road, Yeronga, Brisbane.

Perkins, Ronald George, M.B., B.S., 1947 (Univ. Sydney), General Hospital, Ipswich.

Dique, John Charles Allan, M.B., B.S., 1941 (Univ. Madras), 216 Albany Street, Gosford, New South Wales.

Fullagar, Lesley Joan, M.B., B.S., 1946 (Univ. Melbourne), Rockhampton Hospital, Rockhampton.

Crowley, Hilary Charles Frederick, M.B., B.S., 1948 (Univ. Queensland), 181 Abbotsford Road, Mayne Junction, Brisbane.

Webb, William Kevin, M.B., B.S., 1948 (Univ. Queensland), Abbotsleigh Road, Holland Park, Brisbane.

Zavattaro, Peter, M.B., B.S., 1948 (Univ. Queensland), 62 Qualtrough Street, Buranda, Brisbane.

The following additional qualifications have been registered:

Ryan, James Joseph, 622 Lutwyche Road, Wooloowin, Brisbane, F.R.A.C.S., 1948.

Sinnamon, Cecil Norman, Ryan Road, St. Lucia, Brisbane, D.T.M. and D.T.H. (Univ. Sydney), 1945.

MacPherson, Ronald Kenneth, 66 Barker Street, New Farm, Brisbane, M.D. (Univ. Queensland), 1948.

Obituary.

JAMES SPRENT.

WE are indebted to Dr. W. E. L. H. Crowther for the following appreciation of the late Dr. James Sprent.

James Sprent, who died at Hobart on July 20 last, had played a considerable part in the medical and cultural life of the State. As a Tasmanian of the third generation and a descendant of Mrs. Frances Oates, the first child to be born to free settlers of the First Fleet in New Holland, he had a great pride in his forebears. James Sprent, M.A. (Glasgow), his grandfather, arrived at Hobart by the brig *Norval* in May, 1830, and after a period as proprietor of a boys' school joined the Government Service. He is remembered for his trigonometrical survey of the island and its result, an excellent map published in 1859. A later very accurate survey of Hobart is still referred to in the departments as "Sprent's Bible". Only one of his sons, Charles Percy, grew to manhood and continued his father's work.

C. P. Sprent accomplished much in the field, in the opening up and survey of the mineral areas of our west coast, before his untimely death from typhoid fever, when aged only thirty years. He is still remembered for his relief of the mining settlements when food supplies failed to reach them by sea. Selecting a party, Sprent set out to cut a track through rain forest and unknown country to Mount Bischoff. When, with the more stout-hearted of his men, he got through, all were completely exhausted with their clothing in rags, but in time to send back the required help.

His widow found herself with little means and five children, of whom James was the eldest, to rear and educate. It was a childhood of struggle which left its marks. As James said to me some years ago: "We lived on the smell of an oil rag, and at that time, the iron entered my soul." Leaving the Friends' High School with a scholarship he graduated as a bachelor of science (Tasmania) in 1903. An opportune legacy enabled him to visit Europe, where at the Universities of

Leipzig and Berlin he continued his studies in science and anatomy. From Germany he crossed to Edinburgh and completed the course in medicine in 1909; graduating as a bachelor of medicine and bachelor of surgery with the James Scott prize in midwifery. In his own words: "I was not only a graduate of the University of Edinburgh, I was a scholar." Whilst in Germany he had married, but somehow he managed a period at the Rotunda, Dublin, before returning to Tasmania on appointment as junior house surgeon of the Hobart General Hospital. It was here as a senior student I first met him. He was an impressive person, six feet in height and weighing eighteen stone or more; his dress, ample grey flannels with peg top trousers and a wide-brimmed straw hat, worn well down over his forehead and nose. He had a tremendous "aura". "In Berlin, Crowther, everyone swaggered, but when I passed them in the *Unter den Linden* they all turned to look at me." I believed every word of it. Indeed he suggested power and self-confidence to such a degree that at the hospital, from the four honoraries downward, all were impressed and often disconcerted. His work was well done. Widely read, with a most retentive memory and an interest in pathology that remained with him all his life, he brought new method and thought into the clinical work of the old hospital and set a high standard for his successors.

In 1911 he commenced practice in association with Dr. R. G. Scott, the leading obstetrician. At that time almost all patients were attended in their own homes and fully trained nurses were the exception. Sprent was the first to take with him a modern sterilizer, and his excellent technique brought him much work. Unsuccessful in an election to the Queen Alexandra Hospital, he promptly attained the more attractive one of assistant physician at the General, and on the outbreak of the 1914-1918 war was well established. Service followed with the 3rd and 13th Field Ambulances in the later stages of Gallipoli and on the Somme. For his conduct with the bearers at Mouquet Farm he received the Military Cross. A wound in the chest on the Hindenburg Line, in 1917, brought about his return to Tasmania later in that year, and an appointment as medical officer to the Repatriation Department. His return to private practice followed, but no longer as a general practitioner. The decision to undertake the work of a consulting physician was a bold one, as, owing to the hospital dispute, his honorary position had lapsed. For the remainder of his life he kept rigidly to consultant work in private, in industrial disputes and at the Repatriation Department. He had, however, a strong bias to skin diseases. In these years he was actively concerned in the affairs of the British Medical Association, and in 1920 was President of the Tasmanian Branch.

There soon came a turning point in his life. Having written a letter to the Press on a professional matter, under his signature, he was asked for an explanation. Such a request was intolerable, and he resigned at once from the Association and never returned to it. It was a sad and unnecessary action. Angry and embittered, he withdrew into himself to face grave personal decisions. Keeping doggedly to his work, he made no contributions to meetings or journals and was, in his professional and personal relations, reserved and difficult.

Better times came gradually when, through his friend, S. O. Cowen, he was invited to join the Association of Physicians. Their meetings supplied the great want in his professional life, and when the Royal Australasian College of Physicians was formed he was a Foundation Fellow. For the remainder of his life the College was his principal interest, and from the first he directed its development in Tasmania. Eager to encourage others to work for Membership he is responsible for its considerable numerical increase in this State. He insisted on a high standard of contributions to the annual and clinical meetings at Hobart and Launceston from each Fellow and Member in his turn, and excelled in the chair and at the dinners that followed. Insistent on the social as well as the scientific aspects of the gatherings, his own home was always thrown open and he was the perfect host.

It is a trite saying that we will not see his like again, but Sprent really was unique. He dominated or at least was accorded the full attention of any gathering of his colleagues. Opening his remarks at any meeting with a deep-voiced "Sir", he had its full attention. An excellent speaker, clear and precise, he had a full appreciation of the subject to which he addressed himself. Unfortunately he wrote little and made no contributions to the journals, so there is no record of his attainments or style.

As a consultant, Sprent was correct, formal and most helpful. In his later years, a consultation, at one time dreaded because of his peremptory and overbearing manner, became a delight, as his humanity, wit and real wisdom were revealed. He made his mistakes with the rest of us, but he made remarkable diagnoses and left one happier and better able to conduct a difficult case.

Sprent had a wide background of culture, travel and reading. Behind his gruffness and intolerance there was a sensitive, almost romantic, idealism, and on occasion he found his expression in verse. A notable example was the occasion when the Tasmanian Club "dined" his son, a sergeant in a tank-attack unit, and other servicemen when on furlough on their return from the Middle East.

With Mrs. Sprent he had formed a remarkable collection of china, which became a great solace as his health failed. It was their custom during the war to exhibit and explain their rarities to selected parties, and they thus made it of material help to the Red Cross.

A great club man, he enjoyed billiards and racing. At all times a gourmet and lover of good wine, he liked best a well-chosen dinner at his own home with the company in full harmony with the entertainment, and his fortunate guests will long remember them.

For the last few years increasing cardio-vascular difficulties had been borne with exemplary courage, and only a few days before his death he dragged himself to a meeting of the Medical Council of Tasmania and took part in its proceedings, although so dyspnœic at first as to be hardly able to speak.

At the last "all ranks" dinner of the Tasmanian Club, his place was empty. His friend C.E.F. contributed a valedictory in verse which each guest found in his place. With his consent, I have taken these extracts to close my own expression of personal affection.

Honest, rugged, testy, true,
Truculent, if need be, too.
. . . .

Judge of men, cigars and books,
Wine and song, and food and cooks,
With him manners made the man.
. . . .

If he were with us tonight,
How he'd beam with bland delight,
That the man he thought of most
Drank a little silent toast,
To Jimmy.

REGINALD ARTHUR PARKER.

DR. REGINALD ARTHUR PARKER died on November 30, 1948, and was buried privately at Spring Vale Cemetery. He was born at Hobart in 1876 and was in the service of the Union Bank in that city for six years before commencing the medical course at the University of Sydney. He graduated from the medical school of that university in 1907 and went to Perth to an appointment as resident medical officer; he subsequently occupied the senior resident post at the Perth Hospital.

Dr. Parker started in private pratice at Mildura and was in medical charge of the Mildura District Hospital. During six years in that town he not only was the doctor but became the first president of the lawn tennis association and of the Mildura Rowing Club.

On returning from a trip to England, Dr. Parker settled in medical practice at Healesville and again undertook public duties of a varied nature. He was president of the bowling club for five years and of the tennis club for two years. As a member of the Healesville Shire Council and a commissioner of the Water Trust, he took an active part in the introduction of electric light. He was a foundation member of the Healesville masonic lodge and its first junior warden. Dr. Parker also conducted a choir and became president of the Healesville Shire.

A few years ago, Dr. Parker retired from practice and came to live at 140 Sackville Street, East Kew, but, though in ill health, he rendered splendid service as chairman and president for over seven years at the Victorian Benevolent Home. He was also a justice of the peace and served on the Kew bench, was president of the Camberwell Bowling Club, and after the outbreak of war did honorary medical work at the Alfred, Prince Henry's and the Royal Melbourne hospitals for as long as his health permitted.

Dr. Parker sang first bass in the Victorian Liedertafel and was a member of several cathedral choirs. He was also a lecturer and examiner for the Saint John's Ambulance Association at Mildura and at Healesville, and was a member of the Melbourne Chess Club. Since 1942 he had been living privately at 63 Burke Road, East Malvern; he is survived by his widow and a daughter, to whom we extend our sympathy.

JAMES MACDONALD GILL.

We regret to announce the death of Dr. James Macdonald Gill, which occurred on January 11, 1949, at Gordon, New South Wales.

KEITH McKEDDIE DOIG.

We regret to announce the death of Dr. Keith McKeddie Doig, which occurred on January 3, 1949, at Melbourne.

CLIVE HENRY SIPPE.

We regret to announce the death of Dr. Clive Henry Sippe, which occurred on January 16, 1949, at Brisbane.

Nominations and Elections.

The undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Grant, Alexander John, M.B., 1947 (Univ. Sydney), 72 Norfolk Road, Epping.
Mason, John Herbert, M.B., B.S., 1948 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.
Lamond, Paul Kenneth, M.B., B.S., 1948 (Univ. Sydney), 15 Bayview Crescent, Annandale.
Walter, Clement Jack, M.B., B.S., 1947 (Univ. Sydney), 442 Mowbray Road, Lane Cove.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Beirman, Basil Nathan, M.B., B.S., 1948 (Univ. Sydney), 9 Roe Street, Bondi North.
Burke, William John Gerard, M.B., B.S., 1946 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.
Coolican, Raphael Francis Edward, M.B., B.Ch., 1947 (Univ. Dublin), Richard Street, Bourke.
Hanks, Thomas James, M.B., B.S., 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Lyall, John Angus, M.B., 1947 (Univ. Sydney), Adelong.
Mathers, Peter, M.B., B.S., 1939 (Univ. Sydney), 73 Todman Avenue, Kensington.
Newton, Helen Shackfield, M.B., B.S., 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Stuckey, Gordon Clarence, M.B., B.S., 1948 (Univ. Sydney), Maitland District Hospital, West Maitland.
Sussman, Ewen, M.B., B.S., 1946 (Univ. Sydney), Women's Hospital, Crown Street, Sydney.
Tully, John Kitching, M.B., B.S., 1948 (Univ. Sydney) (Provisional Registration), 191 Mowbray Road, Willoughby.

Notice.

The quarterly meeting of the Section of Allergy of the New South Wales Branch of the British Medical Association will be held in the William H. Crago Council Chamber, British Medical Association House, 135 Macquarie Street, Sydney, on Friday, February 4, 1949, at 4.30 o'clock p.m. The subject for discussion will be "Histamine in Allergy". An invitation is extended to any member of the Association to be present.

Medical Appointments.

Dr. Freda Evelyn Gibson has been appointed Quarantine Officer at Levenard, South Australia, under the *Quarantine Act*, 1908-1947.

Dr. J. J. McIntosh has been appointed Government Medical Officer at Mareeba, Queensland.

Dr. A. Fryberg, Dr. J. I. Tonge, Dr. A. J. Canny, Dr. A. D. D. Pye, Dr. G. C. Taylor and Dr. W. H. Steel have been appointed Members of the Council of the Queensland Institute of Medical Research in pursuance of the provisions of *The Queensland Institute of Medical Research Act of* 1945.

Dr. A. D. D. Pye has been appointed Deputy Chairman of the Council of the Queensland Institute of Medical Research in pursuance of the provisions of *The Queensland Institute of Medical Research Act of* 1945.

Diary for the Month.

FEB. 1.—New South Wales Branch, B.M.A.: Organization and Science Committee (with representatives of Special Groups).
FEB. 2.—Western Australian Branch, B.M.A.: Council Meeting.
FEB. 2.—Victorian Branch, B.M.A.: Branch Meeting.
FEB. 3.—South Australian Branch, B.M.A.: Council Meeting.
FEB. 4.—Queensland Branch, B.M.A.: Branch Meeting.
FEB. 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEB. 10.—Victorian Branch, B.M.A.: Organization Sub-committee.
FEB. 11.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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